A Phase Ib study to assess safety, tolerability, pharmacokinetics, and preliminary antitumor activity of sitravatinib in combination with tislelizumab in patients with advanced solid tumors

Jeffrey Goh, Ben Gao, Ben Markman, Hui Gan, Mark Voskoboynik, Yi-Long Wu, Jun Guo, Qing Zhou, Jun Zhao, Cheng Chen, Jingjun Qiu, Yingying Xu, Liu Yang, and Michael Millward

Abstract

Background: Sitravatinib is an investigative, orally bioavailable, spectrum-selective receptor tyrosine kinase (RTK) inhibitor with potential antitumor activity that has been shown to potently inhibit split kinase receptors (eg, VEGFR2, KIT) and TAM receptors (eg, AXL, MER). Inhibition of RTKs by sitravatinib may also modulate effects on the tumor microenvironment to overcome resistance to checkpoint inhibitors, including enhanced M1/suppressed M2 macrophage cytokine response, abrogated negative regulation of antitumor NK cell activity, and depleted regulatory T- and myeloid-derived suppressor cells with enhanced antitumor cytotoxic T-cell activity. 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). Combining an agent that has both immune modulatory and antitumor properties with an immunotherapeutic PD-1 checkpoint inhibitor could enhance the antitumor efficacy

observed with either agent alone. The primary objective of this trial is to examine the safety and tolerability of sitravatinib combined with tislelizumab in patients with advanced solid tumors.

Methods: Adult patients with histologically or cytologically confirmed, locally advanced or metastatic, non-small cell lung cancer (NSCLC), renal cell carcinoma (RCC), or ovarian cancer (OC) 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 patients will receive sitravatinib 120 mg PO QD in combination with tislelizumab 200 mg IV Q3W until progressive disease, unacceptable toxicity, death, withdrawal of consent, or study termination by the sponsor. Approximately 100 patients are expected to be enrolled in 5 cohorts (n=20 patients per cohort): Cohort A: anti-PD-(L)1 antibody-refractory/-resistant, metastatic, nonsquamous 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 RCC; Cohort D (China only): metastatic or advanced RCC without prior therapy; Cohort E: anti-PD-(L)1 antibody-naive, recurrent, platinum-resistant, epithelial OC. The primary endpoint is to assess safety and tolerability of the combination 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. Seven patients have enrolled as of 3 January 2019 at the sites in Australia and China.

Clinical trial registry number: NCT03666143

Citation Format: Jeffrey Goh, Ben Gao, Ben Markman, Hui Gan, Mark Voskoboynik, Yi-Long Wu, Jun Guo, Qing Zhou, Jun Zhao, Cheng Chen, Jingjun Qiu, Yingying Xu, Liu Yang, Michael Millward. A Phase Ib study to assess safety, tolerability, pharmacokinetics, and preliminary antitumor activity of sitravatinib in combination with tislelizumab in patients with advanced solid tumors [abstract]. In: Proceedings of the American Association for Cancer Research Annual Meeting 2019; 2019 Mar 29-Apr 3; Atlanta, GA. Philadelphia (PA): AACR; Cancer Res 2019;79(13 Suppl):Abstract nr CT167.