China subgroup results of the phase (Ph) 2b HERIZON-BTC-01 study: Zanidatamab in previously-treated HER2-amplified biliary tract cancer (BTC)

Authors: Huichuan Sun[1*], Lequn Bao[2], Jieer Ying[3], Feng Xie[4], Hongming Pan[5], Guohua Yu[6], Xiaoyu Yin[7], Tianqiang Song[8], Kainan Li[9], Qiang Yan[10], Xiaotian Wu[11], Yuanyuan Bao[12], Phillip Garfin[13], Yi Zhao[14], Jia Fan[15**]

Affiliations: [1]Department of Liver Surgery and Transplantation, Affiliated Zhongshan Hospital of Fudan University, Shanghai, China; [2]Department of Hepatobiliary and Pancreatic Surgery, Hubei Cancer Hospital, Wuhan City, China; [3]Department of Medical Oncology, Zhejiang Cancer Hospital, Hangzhou, China; [4]Department of Biliary Tract Surgery III, Eastern Hepatobiliary Surgery Hospital, Affiliated to Naval Medical University, Shanghai, China; [5]Department of Oncology, Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou, China; [6]Department of Oncology, Weifang People's Hospital, Weifang, China; [7]Department of Pancreato-biliary Surgery, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China; [8]Department of Hepatobiliary Cancer, Tianjin Medical University Cancer Institute and Hospital, Tianjin, China; [9]Department of Oncology, Shandong Provincial Third Hospital, Cheeloo College of Medicine, Shandong University, Shandong, China; [10]Department of Hepatobiliary Surgery, Huzhou Central Hospital, Huzhou, China; [11]Biostatistics, Jazz Pharmaceuticals, Palo Alto, CA, United States of America; [12]Statistics, BeiGene (Shanghai) Co., Ltd., Shanghai, China**;** [13]Department of Clinical Research, Hematology/Oncology, Jazz Pharmaceuticals, Palo Alto, CA, United States of America; [14]Clinical Development, BeiGene (Beijing) Co., Ltd., Beijing, China; [15]Department of Liver Surgery and Transplantation, Affiliated Zhongshan Hospital of Fudan University, Shanghai, China.

ABSTRACT

Objectives: Patients with advanced biliary tract cancer (BTC) have a poor prognosis. Approximately one-fifth of all new cases globally are diagnosed in China. Treatment options after gemcitabine failure are limited to chemotherapeutic agents for patients without targetable mutations. Zanidatamab is a HER2-targeted bispecific antibody that binds to two non-overlapping HER2 domains and crosslinks neighboring HER2 proteins. The antitumor activity of zanidatamab monotherapy is being investigated in the ongoing multicenter, open-label, single-arm, phase 2b HERIZON-BTC-01 study (NCT04466891). In the primary and updated analyses, zanidatamab demonstrated a meaningful clinical benefit with a manageable safety profile in patients with treatment-refractory HER2+ BTC. Here, we present the efficacy and safety results for the participants enrolled in Cohort 1 (HER2 immunohistochemistry 2+ or 3+) from China at the data cutoff of July 28, 2023.

Methods: Enrolled patients were adults diagnosed with HER2-amplified, unresectable, locally advanced or metastatic BTC. Additional eligibility criteria included ≥1 prior systemic therapy for advanced disease including gemcitabine and experiencing progressive disease/intolerance following the most recent prior therapy. All patients received zanidatamab monotherapy (20 mg/kg IV Q2W). The primary endpoint was the confirmed objective response rate (ORR) as assessed by independent central review (ICR) per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. Select secondary endpoints were ICR-assessed disease control rate (DCR), duration of response (DoR), percentage of DoR ≥16 weeks, and progression-free survival (PFS), in addition to overall survival (OS) and adverse events (AEs).

Results: Twenty-two patients were enrolled in Cohort 1 (N=80 patients globally) from China. The median age was 59.5 years (range 42-79); 15 patients (68.2%) presented with gallbladder cancer, 4 patients (18.2%) with intra-hepatic and 3 patients (13.6%) with extra-hepatic cholangiocarcinoma,

respectively. The median number of prior treatment regimens received for metastatic or locally advanced disease was 1 (range 1-5). As of July 28, 2023, the median duration of study follow-up was 19.8 months (range 16.5-26.3), with 2 patients (9.1%) remaining on study treatment. The confirmed ORR assessed by ICR was 40.9% (95% CI, 20.7-63.6), 9 patients (40.9%) had confirmed partial response (PR), and 9 (40.9%) had stable disease. The DCR was 81.8% (95% CI, 59.7-94.8). The median DoR was 11.2 months (95% CI: 3.9-not estimable). Among confirmed responders, 7 patients (77.8%) had a response duration of ≥16 weeks. The median PFS was 6.2 months (95% CI, 3.3-7.6), and median OS was 11.2 months (95% CI, 8.5-18.7). Sixteen patients (72.7%) experienced ≥1 treatment-related adverse events (TRAEs). The most common TRAEs were infusion-related reaction (36.4%) and diarrhea (31.8%), most of which were grade 1 or 2 events. A total of 6 patients (27.3%) experienced ≥1 grade 3 or higher TRAEs, and 3 patients (13.6%) experienced serious TRAEs. Only 1 patient (4.5%) reported a confirmed treatment-emergent cardiac event. There was no treatment-related patient discontinuation due to adverse events. No adverse event leading to death was reported.

Conclusions: Zanidatamab monotherapy demonstrated a clinically meaningful benefit for Chinese patients with treatment-refractory HER2+ BTC, consistent with findings in the primary analyses. Zanidatamab treatment was also well tolerated with manageable adverse events.