Asia subgroup overall survival and long-term follow-up results of the phase 2b HERIZON-BTC-01 study: Zanidatamab in previously treated human epidermal growth factor receptor 2-amplified biliary tract cancer

Authors: Do-Youn Oh[1]*; Huichuan Sun[2]; Jin Won Kim[3]; Hye Jin Choi[4]; Heung-Moon Chang[5]; Lequn Bao[6]; Jieer Ying[7]; Feng Xie[8]; Myung-Ah Lee[9]; Young Mi Seol[10]; Xiaotian Wu[11]; Yuanyuan Bao[12]; Phillip Garfin[13]; Yi Zhao[14]; Jia Fan[2]**

Affiliations: [1]Department of Internal Medicine, Seoul National University Hospital, Cancer Research Institute, Seoul National University College of Medicine, Seoul, Republic of Korea; [2]Department of Liver Surgery and Transplantation, Affiliated Zhongshan Hospital of Fudan University, Shanghai, China; [3]Department of Internal Medicine, Seoul National University Bundang Hospital, Seoul, Republic of Korea; [4]Department of Internal Medicine, Severance Hospital Yonsei University Health System, Seoul, Republic of Korea; [5]Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; [6]Department of Hepatobiliary and Pancreatic Surgery, Hubei Cancer Hospital, Wuhan City, China; [7]Department of Medical Oncology, Zhejiang Cancer Hospital, Hangzhou, China; [8]Department of Biliary Tract Surgery III, Eastern Hepatobiliary Surgery Hospital, Affiliated to Naval Medical University, Shanghai, China; [9]Division of Medical Oncology, Department of Internal Medicine, The Catholic University of Korea, Seoul St. Mary's Hospital, Seoul, Republic of Korea; [10]Department of Internal Medicine, Pusan National University Hospital, Pusan National University College of Medicine, Busan, Republic of Korea; [11]Department of Data Science, Jazz Pharmaceuticals, Palo Alto, CA, United States of America; [12]Clinical Development, BeOne Medicines, Ltd, Shanghai, China; [13]Department of Clinical Research, Hematology/Oncology, Jazz Pharmaceuticals, Palo Alto, CA, United States of America; [14]Clinical Development, BeOne Medicines, Ltd, Beijing, China.
*Lead and presenting author **Corresponding Author

ABSTRACT

Background: In patients with previously treated human epidermal growth factor receptor 2 (HER2+) biliary tract cancer (BTC), HER-2 targeted zanidatamab demonstrated a meaningful clinical benefit with a manageable safety profile in the overall population and Asia subgroup (HERIZON-BTC-01 trial, NCT04466891). Here, we report updated analyses and overall survival for Cohort 1 (HER2-amplified with either immunohistochemistry 2+ or 3+) from the Asia subgroup (China and South Korea).

Methods: This open-label, phase 2b study enrolled adults with HER2-amplified, unresectable, locally advanced/metastatic BTC, and ≥1 prior gemcitabine-containing systemic therapy. Patients received zanidatamab monotherapy (20 mg/kg intravenously every 2 weeks). The primary endpoint was confirmed objective response rate and select secondary endpoints were duration of response, progression-free survival, overall survival, and adverse events.

Results: Cohort 1 enrolled 50 patients from Asia. Baseline demographic and disease characteristics were stated previously. As of July 28, 2023, 4 patients (8%) remained on treatment; median study follow-up was 20.8 months (range 16.5-31.9). Efficacy data is presented in the table. Thirty-five patients (70%) experienced ≥1 treatment-related adverse events (TRAEs); most common were infusion-related reaction (42%) and diarrhea (28%). Seven patients (14%) experienced ≥1 grade 3 or higher TRAEs, most common was ejection fraction decreased (4%); 3 patients (6%) experienced

serious TRAEs. One patient (2%) had a TRAE leading to treatment discontinuation; no TRAE leading to death was reported.

Conclusions: With longer follow-up, zanidatamab demonstrated extended response with an encouraging median overall survival for patients from Asia with previously treated HER2+ BTC and remained well tolerated with manageable adverse events.

Table:

	Asia subgroup (n=50)
Objective response rate[a], % (95% CI)[b]	42 (28-57)
Median duration of response, months (95% CI)[c]	11.2 (3.9-not estimable)
Duration of response ≥16 weeks, n (%) (95% CI)[b]	17 (81) (58-95)
Median progression-free survival, months (95% CI)[c]	5.5 (3.3-7.2)
Median overall survival, months (95% CI)[c]	13.4 (9.7-18.1)
12-month overall survival, % (95% CI)[d]	54 (38-67)

[a]Confirmed by independent central review per RECIST v1.1. 95% CI estimated using methods:

[b]Clopper-Pearson exact binomial.

[c]Brookmeyer & Crowley with log-log transformation.

[d]Greenwood.

CI, confidence interval; RECIST, Response Evaluation Criteria in Solid Tumors.