Zanidatamab (ZW25; Zani) in Patients (pts) with Previously Treated Advanced Human Epidermal Growth Factor Receptor 2 (HER2)-Amplified Biliary Tract Cancer (BTC): Asia Subgroup Analysis of the Phase 2b HERIZON-BTC-01 Study

Authors: H. Sun[1], J.W. Kim[2], H.J. Choi[3], H.-M. Chang[4], L. Bao[5], J. Ying[6], F. Xie[7], M.A. Lee[8], K. Dong Uk[9], T. Song[10], H. Pan[11], G. Yu[12], K. Li[13], Q. Yan[14], X. Wu[15], Y. Bao[16], P. Garfin[17], J. Ma[18], J. Fan[1], D.-Y. Oh[19];

[1]Department of Liver Surgery and Transplantation, Affiliated Zhongshan Hospital of Fudan University, Shanghai, China, [2]Department of Internal Medicine, Seoul National University Bundang Hospital, Seoul, Korea, Republic of, [3]Department of Internal Medicine, Severance Hospital Yonsei University Health System, Seoul, Korea, Republic of, [4]Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, Republic of, [5]Department of Hepatobiliary and Pancreatic Surgery, Hubei Cancer Hospital, Wuhan City, China, [6]Department of Medical Oncology, Zhejiang Cancer Hospital, Hangzhou, China, [7]Department of Biliary Tract Surgery III, Eastern Hepatobiliary Surgery Hospital, Affiliated to Naval Medical University, Shanghai, China, [8]Division of Medical Oncology, Department of Internal Medicine, The Catholic University of Korea, Seoul St. Mary's Hospital, Seoul, Korea, Republic of, [9]Department of Gastroenterology, Pusan National University Hospital, Busan, Korea, Republic of, [10]Department of Hepatobiliary Cancer, Tianjin Medical University Cancer Institute and Hospital, Tianjin, China, [11]Department of Oncology, Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou, China, [12]Department of Oncology, Weifang People's Hospital, Weifang, China, [13]Department of Oncology, Shandong Provincial Third Hospital, Cheeloo College of Medicine, Shandong University, Shandong, China, [14]Department of Hepatobiliary Surgery, Huzhou Central Hospital, Huzhou, China, [15]Department of Data Science, Jazz Pharmaceuticals, Palo Alto, CA, United States of America, [16]Clinical Development, BeiGene (Shanghai) Co., Ltd., Shanghai, China, [17]Department of Clinical Research, Hematology/Oncology, Jazz Pharmaceuticals, Palo Alto, CA, United States of America, [18]Clinical Development, BeiGene (Beijing) Co., Ltd., Beijing, China, [19]Department of Internal Medicine, Seoul National University Hospital, Cancer Research Institute, Seoul National University College of Medicine, Seoul, Korea, Republic of

Background

Zani, a HER2-targeted bispecific antibody, has shown antitumor activity and a tolerable and manageable safety profile in pts with HER2-amplified, treatment (Tx)-refractory, advanced BTC (HERIZON-BTC-01; NCT04466891). Here, we report a post-hoc analysis of the Asia subgroup in predetermined cohort 1 (HER2 immunohistochemistry 2+ or 3+) comprising pts from China and South Korea.

Methods

This phase 2b, open-label, single-arm study evaluated zani monotherapy (20 mg/kg IV Q2W) in adults with HER2-amplified, inoperable, locally advanced/metastatic BTC. Pts had received ≥1 prior systemic Tx for advanced disease, including gemcitabine. The primary endpoint was confirmed objective response rate. Secondary endpoints included disease control rate, duration of response, progression-free survival, and adverse events (AEs).

Results

Of 80 pts enrolled in cohort 1, 50 were from Asia (median age 63.5 years; 29 [58%] gallbladder cancer, 11 [22%] intra-, and 10 [20%] extra-hepatic cholangiocarcinoma). At data cutoff (Oct 10, 2022), median study follow-up was 11.3 months (range 6.9-22.3); 7 (14%) pts remained on Tx. Pts had median 1 prior line (range 1-5) of Tx for advanced disease. Efficacy is summarized in Table 1. Tx-related AEs (TRAEs) were experienced by

70% of pts, the most common being infusion-related reactions (42%), diarrhea (28%), and decreased ejection fraction (EF; 12%). In all, 10% of pts experienced grade 3 TRAEs (decreased EF [4%]; diarrhea, increased blood bilirubin, and enteritis [all 2%]); none had grade 4/5 TRAEs. A total of 4% of pts had serious TRAEs and 2% discontinued Tx due to decreased EF.

	Asia subgroup (n=50)
Objective response rate[a], % (95% CI)[b]	42 (28, 57)
Best overall response[a], n (%)	
Complete response	0 (0)
Partial response	21 (42)
Stable disease	13 (26)
Progressive disease	15 (30)
Not evaluable	1 (2)
Disease control rate[a], % (95% CI)[b]	68 (53, 81)
Median duration of response, months (95% CI)[c]	7.4 (3.9, not estimable)
Duration of response ≥16 weeks, n (%) (95% CI)[b]	16 (76) (53, 92)
Median progression-free survival, months (95% CI)[c]	5.5 (3.3, 7.0)

CI, confidence interval

[a]Confirmed by independent central review per RECIST v1.1; [b]Estimated using Clopper-Pearson method; [c]Estimated using Brookmeyer & Crowley method with log-log transformation.

Conclusions

Zani demonstrated durable tumor responses and a tolerable and manageable safety profile in pts in the Asia subgroup with Tx-refractory HER2- amplified advanced BTC, consistent with the overall study population (Harding J, et al. Lancet Oncol. 2023).