**Zanidatamab (zani), a HER2-targeted bispecific antibody, in combination with docetaxel as first-line therapy (1L) for patients (pts) with advanced HER2-positive breast cancer (BC): updated results from a Phase Ib/II study**

**Authors:** Xiaojia Wang,[1] Keun Seok Lee,[2] Xiaohua Zeng,[3] Tao Sun,[4] Young-Hyuck Im,[5] Huiping Li,[6] Kun Wang,[7] Huiyan Li,[8] Ping Zhou,[8] Yuanyuan Bao,[8] and Zefei Jiang[9]

**Affiliations:** *[1]Department of Oncology, Zhejiang Cancer Hospital, Hangzhou, China; [2]Department of Oncology, National Cancer Center, Goyang-si, Republic of Korea; [3]Department of Breast Oncology, Chongqing University Cancer Hospital, Chongqing, China; [4]Department of Breast Oncology, Liaoning Cancer Hospital, Liaoning, China; [5]Department of Oncology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [6]Department of Breast Oncology, Beijing Cancer Hospital, Beijing, China; [7]Department of Breast Cancer, Cancer Center, Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences), Southern Medical University, Guangzhou, China; [8]Clinical Development, BeiGene (Shanghai) Co., Ltd., Shanghai, China; [9]The Fifth Medical Center of Chinese PLA General Hospital, Beijing, China*

**Background:** Despite HER2-targeted agents improving outcomes in HER2-positive (+) BC, some pts develop resistance, relapse, or do not respond to current 1L therapies. Zani, also known as ZW25, is a novel HER2-targeted bispecific antibody that binds to two distinct extracellular domains of HER2. Preliminary results from this Phase Ib/II trial (NCT04276493) showed that zani plus docetaxel had a manageable safety profile and demonstrated promising antitumor activity in pts with advanced HER2+ BC; here we present the updated data following enrollment completion.

**Methods:** Cohort 1 of this open-label study is evaluating zani in combination with docetaxel as a 1L therapy in adult females with advanced HER2+ BC who may have received prior neoadjuvant/adjuvant therapy. Cohort 1a pts received zani 30 mg/kg intravenously (IV), Cohort 1b pts received zani 1800 mg IV, both with docetaxel 75 mg/m$^2$ IV every 3 weeks. The primary endpoints were safety and investigator (INV)-assessed objective response rate (ORR) per RECIST v1.1. Secondary endpoints included INV-assessed duration of response (DoR) and disease control rate (DCR).

**Results:** As of Nov 22, 2022, 37 pts (median age 55.0 years [range: 33-80]) were assigned to Cohort 1a (n=10) or 1b (n=27). Median study follow-up was 15.5 months (range: 1.1-29.3); patients received a median of 13 treatment cycles (range 1-37) and 18 (48.6%) pts remained on treatment. Of the 33-efficacy evaluable (EE) pts, confirmed ORR was 90.9% (95% confidence interval [CI]: 75.7, 98.1).

Efficacy data are summarized in Table 1. In total, 36 (97.3%) pts experienced ≥1 treatment-related adverse event (TRAE); 25 (67.6%) pts experienced ≥grade 3 TRAEs. The most common ≥grade 3 TRAEs were decreased neutrophil count, experienced by 18 (48.6%) pts, and decreased white blood cell count, experienced by 7 (18.9%) pts. Serious TRAEs occurred in 6 (16.2%) pts; no TRAEs led to death.

**Conclusions:** Zani combined with docetaxel demonstrated promising antitumor activity as 1L therapy for advanced HER2+ BC, with a manageable safety profile.

**Table 1. Summary of efficacy results (EE analysis set*)**

| | **Cohort 1a (n=8)** | **Cohort 1b (n=25)** | **Total (n=33)** |
|---|---|---|---|
| **Confirmed best overall response, n (%)** | | | |
| Complete response | 1 (12.5) | 1 (4.0) | 2 (6.1) |
| Partial response | 7 (87.5) | 21 (84.0) | 28 (84.8) |
| Stable disease | 0 (0.0) | 2 (8.0) | 2 (6.1) |
| Progressive disease | 0 (0.0) | 1 (4.0) | 1 (3.0) |
| **Confirmed ORR, n (%)** | 8 (100) | 22 (88.0) | 30 (90.9) |
| **95% CI** | 63.1, 100 | 68.8, 97.5 | 75.7, 98.1 |
| **Confirmed DCR, n (%)** | 8 (100) | 24 (96.0) | 32 (97.0) |
| **95% CI** | 63.1, 100 | 79.6, 99.9 | 84.2, 99.9 |
| **Median DoR, months** | 12.4 | NE | NE |
| **(95% CI)** | 5.5, NE | 12.1, NE | 12.1, NE |
| **Confirmed DoR, range**† | 3.5†-23.5† | 4.3†-16.5† | 3.5†-23.5† |

*Four pts without any postbaseline tumor assessments were excluded from the EE analysis set

Data cut off: November 22, 2022

† Censored