Zanidatamab (zani), a HER2-targeted bispecific antibody, in combination with docetaxel as first-line (1L) therapy for patients (pts) with advanced HER2-positive breast cancer: Preliminary results from a Phase 1b/2 study

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

Affiliations: *[1]National Cancer Center, Center for Breast Cancer, Goyang, Republic of (South) Korea; [2]Department of Oncology, Zhejiang Cancer Hospital, Hangzhou, China; [3]Department of Oncology, Samsung Medical Center, Sungkyunkwan University* School *of Medicine, Seoul, Republic of (South) Korea; [4]Department of Breast Cancer Center, Chongqing University Cancer Hospital, Chonqqing, China; [5]Department of Breast Oncology, Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Peking University Cancer Hospital & Institute, Beijing, China; [6]Department of Breast Cancer, Cancer Center, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, Guangzhou, China; [7]BeiGene (Shanghai) Co., Ltd., Shanghai, China; [8]The Fifth Medical Center of Chinese PLA General Hospital, Beijing, China*

Abstract:

Background: HER2-targeted agents have improved outcomes in HER2-positive breast cancer, but 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. In a Phase 1 trial (NCT02892123) zani was well tolerated and demonstrated preliminary antitumor activity as monotherapy/with chemotherapy in pts with pre-treated advanced HER2+ breast cancer.

Methods: Cohort 1 of this ongoing open-label, Phase 1b/2 study (NCT04276493) is evaluating zani in combination with docetaxel as a 1L therapy in adult females with advanced HER2+ breast cancer who may have received prior neoadjuvant/adjuvant treatment. Cohort A pts received zani 30 mg/kg IV, Cohort B pts received zani 1800 mg IV, both with docetaxel 75 mg/m^2 IV Q3W. 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), disease control rate (DCR) and progression-free survival (PFS).

Results: As of Nov 26, 2021, 25 pts with a median age of 57.0 years (range: 33.0–80.0) were assigned to Cohort A (n=11) or B (n=14). Median study follow-up was 7.0 months (range: 1.1–17.4) and the median number of treatment cycles was 10 (range: 2–20), 16 (64.0%) pts remained on treatment. Of the 22-efficacy evaluable (EE) pts, confirmed ORR was 86.4% (95% CI: 65.1, 97.1). The 6 months PFS rate was 90.9% (95% CI: 68.3, 97.7). Efficacy data are summarized in Table 1. All pts experienced ≥ 1 treatment emergent adverse event (TEAE) and 17 (68.0%) pts experienced ≥ Grade 3 TEAEs. In total, 23 (92.0%) pts experienced treatment related TEAEs (trTEAEs), and 17 (68.0%) pts experienced ≥ Grade 3 trTEAEs. The most common trTEAEs were diarrhea (56.0%) and decreased neutrophil count (52.0%). Serious trTEAEs occurred in two (8.0%) pts, trTEAEs leading to treatment discontinuation occurred in one (4.0%) pt and no trTEAEs led to death.

Conclusions: Zani and docetaxel combination demonstrated antitumor activity in 1L therapy for advanced HER2+ breast cancer, with a manageable safety profile.

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

	Cohort A (n=9)	**Cohort B (n=13)**	**Total (n=22)**
Confirmed best overall response, n (%)			
Complete response	1 (11.1)	0 (0)	1 (4.5)
Partial response	7 (77.8)	11 (84.6)	18 (81.8)
Stable disease	0 (0)	1 (7.7)	1 (4.5)
Progressive disease	1 (11.1)	1 (7.7)	2 (9.1)
Confirmed ORR, n (%)	8 (88.9)	11 (84.6)	19 (86.4)
95% CI	51.8, 99.7	54.6, 98.1	65.1, 97.1
Confirmed DCR, n (%)	8 (88.9)	12 (92.3)	20 (90.9)
95% CI	51.8, 99.7	64.0, 99.8	70.8, 98.9
Confirmed DoR, range	1.4–12.4	1.5–5.6	1.4–12.4
*Three pts without any post-baseline tumor assessments were excluded from EE analysis set Data cut off: Nov 26, 2021			