

**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**

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**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<sup>2</sup> 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  $\geq 1$  treatment-related adverse event (TRAE); 25 (67.6%) pts experienced  $\geq$  grade 3 TRAEs. The most common  $\geq$  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\*)**

	<b>Cohort 1a (n=8)</b>	<b>Cohort 1b (n=25)</b>	<b>Total (n=33)</b>
<b>Confirmed best overall response, n (%)</b>			
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)
<b>Confirmed ORR, n (%)</b>	8 (100)	22 (88.0)	30 (90.9)
<b>95% CI</b>	63.1, 100	68.8, 97.5	75.7, 98.1
<b>Confirmed DCR, n (%)</b>	8 (100)	24 (96.0)	32 (97.0)
<b>95% CI</b>	63.1, 100	79.6, 99.9	84.2, 99.9
<b>Median DoR, months (95% CI)</b>	12.4 5.5, NE	NE 12.1, NE	NE 12.1, NE
<b>Confirmed DoR, range<sup>†</sup></b>	3.5 <sup>†</sup> -23.5 <sup>†</sup>	4.3 <sup>†</sup> -16.5 <sup>†</sup>	3.5 <sup>†</sup> -23.5 <sup>†</sup>
*Four pts without any postbaseline tumor assessments were excluded from the EE analysis set Data cut off: November 22, 2022 <sup>†</sup> Censored			