Zanidatamab, a HER2-targeted bispecific antibody, in combination with docetaxel as first-line therapy for patients with advanced HER2-positive breast cancer: Updated results from a Phase Ib/II study

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ABSTRACT

Objective: Despite HER2-targeted agents improving outcomes in HER2-positive breast cancer, some patients develop resistance, relapse, or do not respond to current first-line therapies. Zanidatamab, 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 zanidatamab plus docetaxel had a manageable safety profile and demonstrated promising antitumor activity in patients with advanced HER2-positive breast cancer; here, we present the updated data following enrollment completion.

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

Results: As of Nov 22, 2022, 37 patients (median age 55.0 years [range, 33-80]) were assigned to Cohort 1a (n=10) or Cohort 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%) patients remained on treatment. Of the 33 efficacy-evaluable patients, confirmed ORR was 90.9% (95% confidence interval [CI], 75.7-98.1); two (6.1%) patients had confirmed complete responses, 28 (84.8%) patients had confirmed partial responses, two (6.1%) patients had stable disease, and one (3.0%) patient had progressive disease. The confirmed ORR was 100% (95% CI, 63.1-100) for Cohort 1a (evaluable n=8) and 88.0% (95% CI, 68.6-97.5) for Cohort 1b (evaluable n25). The overall confirmed DCR was 97.0% (95% CI, 84.2-99.9). Median DoR was not reached for the overall cohort (range, 3.5-23.5 months) or Cohort 1b (range, 4.3-16.5 months), and was 12.4 months (range, 3.5-23.5 months) for Cohort 1a). In total, 36 (97.3%) patients experienced at least one treatment-related adverse event (TRAE); 25 (67.6%) patients experienced TRAEs greater than grade 3. The most common TRAEs greater than grade 3 were decreased neutrophil count, experienced by 18 (48.6%) patients, and decreased white blood cell count, experienced by 7 (18.9%) patients. Serious TRAEs occurred in 6 (16.2%) patients; no TRAEs led to death.

Conclusion: Zanidatamab combined with docetaxel demonstrated promising antitumor activity as first-line therapy for advanced HER2-positive breast cancer, with a manageable safety profile.