Combining HER2-targeted agents with chemotherapy has resulted in improved survival and the highly immunogenic nature of HER2.

In a Phase 1 dose-escalation and expansion study, single-agent zanidatamab was generally well tolerated and showed antitumor activity in patients with advanced HER2-positive cancer, patients with gastroesophageal cancer and/or breast cancer had overall response rates (ORR) that ranged from 33% to 39%.

The primary objectives are to assess the safety/tolerability and preliminary antitumor activity (as measured by ORR) of zanidatamab in patients with HER2-positive, locally advanced or metastatic breast cancer, and zanidatamab plus tislelizumab in patients with HER2-positive, unresectable locally advanced or metastatic gastric/gastroesophageal junction adenocarcinoma.

Conclusions

BGB-A317-ZW25 is an ongoing Phase 1/2b study evaluating zanidatamab as a first-line therapy with chemotherapy in patients with HER2-positive, unresectable locally advanced or metastatic breast cancer, or with chemotherapy plus tislelizumab in patients with HER2-positive, unresectable locally advanced or metastatic gastric/gastroesophageal junction adenocarcinoma.

Study design and objectives

- The study design is summarized in Figure 4.
- Approximately 50 patients across 12 centers in Asian countries will be recruited.
- The primary objectives are to assess the safety/tolerability and preliminary antitumor activity (as measured by ORR) of zanidatamab in combination with chemotherapy in cohorts 1a to 1d, and combination with tislelizumab and CAPOX (a multi-agent chemotherapy regimen consisting of capecitabine and oxaliplatin) in cohorts 2a and 2b.
- Secondary objectives are to evaluate the preliminary antitumor activity in each cohort as measured by duration of response (DoR), time to response, progression-free survival (PFS), disease control rate (DCR), and overall survival (OS), as well as patient-reported outcomes.

Methods

Study population

- All eligible patients will be ≥ 18 years, have an Eastern Cooperative Oncology Group performance status ≤ 2, and have measurable lesion(s) per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1.
- Cohort 1: Patients with HER2-positive disease by overexpression and/or gene amplification were determined by investigators or central laboratory, using immunohistochemistry (IHC) or fluorescence in situ hybridization (FISH).
- Cohort 2: Patients with histologically or cytologically confirmed unresectable, locally advanced or recurrent or metastatic HER2-positive, with metastatic gastric/gastroesophageal junction adenocarcinoma.

References

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Acknowledgements

The study was conducted by Bexda, Ltd. Medical writing support for the development of this poster, under the direction of the authors, was provided by Shannon Gelder, MSc, of Healthcare Communications, and headed by Bexda, Ltd.

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