TPS648 Trials in Progress Poster Session

HERIZON-BTC-302: A phase 3 study of zanidatamab with standard-of-care (SOC) therapy vs SOC alone for first-line treatment of human epidermal growth factor receptor 2 (HER2)-positive advanced/metastatic biliary tract cancer (BTC).

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Background: Zanidatamab is a humanized, IgG1-like, HER2-targeted bispecific antibody that simultaneously binds to 2 non-overlapping domains on HER2. Zanidatamab is being investigated for the treatment of HER2-expressing solid tumors, including BTC. In the phase 2 HERIZON-BTC-01 trial, zanidatamab monotherapy demonstrated promising antitumor activity in 80 patients with previously treated HER2-positive BTC. Confirmed objective response rate (cORR) was 41.3% with rapid and durable responses and a manageable safety profile. This phase 3 trial is assessing zanidatamab + SOC therapy vs SOC alone for first-line treatment of HER2-positive advanced/metastatic BTC. **Methods:** This ongoing, global, phase 3, randomized, open-label trial (NCT06282575) is investigating the efficacy and safety of zanidatamab with cisplatin and gemcitabine (CisGem) vs CisGem alone ± a programmed cell death protein-1/ligand 1 (PD-1/L1) inhibitor (pembrolizumab or durvalumab at physician's discretion if locally approved) as first-line treatment for patients with advanced HER2-positive BTC. Eligibility criteria include ≥18 years of age; locally advanced, unresectable, or metastatic HER2-positive BTC by immunohistochemistry and in situ hybridization assay (IHC 3+ or IHC 2+/ISH+); and Eastern Cooperative Oncology Group performance status ≤1. Patients may have received ≤2 cycles of a gemcitabine-based regimen ± pembrolizumab or durvalumab. Prior HER2-targeted therapy is not allowed except for patients who completed it for breast cancer >5 years prior to BTC diagnosis. Eligible patients will be randomized to receive zanidatamab (flat 2-tiered dosing: 1800 mg intravenous [IV; body weight <70 kg] or 2400 mg IV [body weight ≥70 kg] every 3 weeks) + a standard dose of CisGem ± a PD1/L1 inhibitor or CisGem alone ± a PD1/L1 inhibitor (≤8 cycles). The primary endpoint is progression-free survival (PFS) in patients with IHC 3+ tumors. Secondary/exploratory endpoints include overall survival (IHC 3+ subgroup; overall population), PFS (overall population), cORR, incidence and severity of adverse events, and patient-reported outcomes. The study is currently recruiting patients. Clinical trial information: NCT06282575. Research Sponsor: Jazz Pharmaceuticals.