TPS4206 Poster Session

A randomized, double-blinded, international phase III trial comparing HLX22 in combination with trastuzumab and chemotherapy versus trastuzumab and chemotherapy with or without pembrolizumab for first-line treatment for HER2-positive locally advanced or metastatic G/GEJ cancer.

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Background: Combination therapy with trastuzumab and chemotherapy is the first-line systemic treatment for human epidermal growth factor receptor 2 (HER2) positive advanced gastric or gastroesophageal junction (G/GEJ) cancer. Among patients whose tumors express programmed death ligand 1 (PD-L1; defined as combined positive score [CPS] ≥ 1), treatment options also include pembrolizumab plus trastuzumab and chemotherapy. Survival outcomes remain unsatisfactory despite these advances. HLX22 is an anti-HER2 antibody that targets a different epitope than trastuzumab. HLX22 has shown improved progression-free survival (PFS) when added to trastuzumab plus oxaliplatin and capecitabine (XELOX) in a phase 2 study (NCT04908813). Here we present the design of a phase III randomized controlled study. **Methods:** This randomized, double-blind, two-arm phase III clinical study aims to compare the efficacy and safety of HLX22 in combination with trastuzumab and XELOX versus (vs) trastuzumab and XELOX with or without ($\pm$) pembrolizumab in patients with HER2-positive, advanced G/GEJ cancer and no prior antitumor therapy in the advanced setting. Key inclusion criteria include histologically or cytologically confirmed diagnosis of previously untreated, locally advanced unresectable or metastatic HER2-positive G/GEJ adenocarcinoma. Key exclusion criteria include prior use of any HER2-target therapy. Approximately 550 eligible patients will be enrolled from multiple regions across the globe and randomly assigned in a 1:1 ratio to receive HLX22 (15 mg/kg) + trastuzumab + XELOX $\pm$ placebo (for pembrolizumab) or placebo (for HLX22) + trastuzumab + XELOX $\pm$ pembrolizumab. HLX22 will be administered intravenously on Day 1 of each 21-day treatment cycle until loss of clinical benefit, death, intolerable toxicity, withdrawal of informed consent, or other reasons. The stratification factors include HER2 immunohistochemistry (3+ vs 2+), geographic region (Asia vs Europe/North America vs rest of the world), primary tumor site (gastric vs gastroesophageal junction), and tumor PD-L1 expression (CPS < 1 or not evaluable vs $1 \leq$ CPS < 10 vs CPS ≥ 10). The dual primary endpoints are PFS assessed by independent radiology review committee per RECIST v1.1 and overall survival. Secondary endpoints include investigator-assessed PFS, objective response rate, PFS on the subsequent line of therapy, duration of response, safety, pharmacokinetics, immunogenicity, and quality of life. This study is currently open for enrollment and has completed first dose of the first patient. Clinical trial information: NCT06532006. Research Sponsor: Shanghai Henlius Biotech, Inc.