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Updated results of HLX22 plus trastuzumab and XELOX for first-line treatment of human epidermal growth factor receptor 2 (HER2)–positive locally advanced or metastatic gastric/gastroesophageal junction cancer (G/GEJC).

Jin Li, Ning Li, Mudan Yang, Yanqiao Zhang, Diansheng Zhong, Meng Qiu, Linzhi Lu, Xiaoming Hou, Yanru Qin, Guoping Sun, Jun Deng, Zimin Liu, Bo Liu, Yuntao Ma, Jingdong Zhang, Futang Yang, Haoyu Yu, Jing Li, Qingyu Wang, Jun Zhu, HLX22-GC Investigators; Department of Oncology, Shanghai GoBroad Cancer Hospital, Shanghai, China; Department of Medical Oncology, The Affiliated Cancer Hospital of Zhengzhou University & Henan Cancer Hospital, Zhengzhou, China; Department of Gastroenterology, Shanxi Cancer Hospital, Taiyuan, China; Department of Gastrointestinal Medical Oncology, Harbin Medical University Cancer Hospital, Harbin, China; Department of Medical Oncology, Tianjin Medical University General Hospital, Tianjin, China; Department of Abdominal Oncology, West China School of Medicine and West China Hospital, Sichuan University, Chengdu, China; Department of Gastroenterology, Gansu Wuwei Tumour Hospital, Wuwei, China; Department of Medical Oncology, The First Hospital of Lanzhou University, Lanzhou, China; Department of Medical Oncology, The Affiliated Cancer Hospital of Zhengzhou University, Zhengzhou, China; Department of Medical Oncology, The First Affiliated Hospital of Anhui Medical University, Hefei, China; Department of Medical Oncology, The First Affiliated Hospital of Nanchang University, Nanchang, China; Department of Oncology, Affiliated Hospital of Qingdao University, Qingdao, China; Department of Gastroenterology, Shandong Provincial Cancer Hospital, Jinan, China; Department of General Surgery, Gansu Provincial Hospital, Lanzhou, China; Department of Gastroenterology, Liaoning Cancer Hospital & Institute, Shenyang, China; Shanghai Henlius Biotech, Inc., Shanghai, China

Background: HER2-positive (HER2+) G/GEJC accounts for 12–23% of G/GEJC cases. Survival outcomes with combined treatment of trastuzumab and chemotherapy remain unsatisfactory. This phase 2 study is evaluating HLX22 and trastuzumab, which target different HER2 epitopes, combined with XELOX chemotherapy as first-line treatment for patients with advanced G/GEJC. Following the report at ASCO GI Cancers Symposium 2025, here we present updated efficacy and safety results at extended follow-up. **Methods:** Patients with locally advanced or metastatic HER2+ G/GEJC and no prior systemic antitumor therapy were enrolled, and randomized in a 1: 1 ratio to receive either HLX22 + trastuzumab + XELOX or placebo + trastuzumab + XELOX in 3-week cycles. Primary endpoints were independent radiology review committee (IRRC)-assessed progression-free survival (PFS) and objective response rate (ORR) per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. Secondary endpoints included other efficacy and safety endpoints. **Results:** As of December 6, 2024, 62 patients were randomized to the respective groups (31 vs 31), of whom 51 (82.3%) were male. Median follow-up duration was 28.5 and 28.7 months for the respective groups. Major efficacy findings are shown in Table 1. Treatment-emergent adverse events (TEAEs) were reported in 30 (96.8%) and 31 (100%) patients, respectively. TEAEs of grade 3 or higher were observed in 17 (54.8%) and 15 (48.4%) patients. HLX22- or placebo-related TEAE leading to death occurred in 1 (3.2%) patient in the placebo + trastuzumab + XELOX group. One patient (3.2%) in each group reported HLX22/placebo-related TEAEs leading to treatment discontinuation. **Conclusions:** Combination of chemotherapy and dual HER2 blockade with HLX22 and trastuzumab conferred survival benefit to HER2-positive G/GEJC patients along with a manageable safety profile. Clinical trial information: NCT04908813. Research Sponsor: Shanghai Henlius Biotech, Inc.

Updated efficacy*.

	HLX22 + trastuzumab + XELOX (n=31)	placebo + trastuzumab + XELOX (n=31)
Median PFS, months (95% CI)	NR (16.2, NE)	8.3 (5.7, 21.4)
HR (95% CI)	0.2 (0.09, 0.54)	
12-month PFS rate (95% CI)	77.1 (56.0, 89.0)	40.8 (20.4, 60.4)
24-month PFS rate (95% CI)	54.8 (27.3, 75.7)	17.5 (1.6, 48.0)
Confirmed ORR, % (95% CI)	87.1 (70.2, 96.4)	80.6 (62.5, 92.5)
Median OS, months (95% CI)	NR (16.2, NE)	16.4 (10.7, NE)
HR (95% CI)	0.6 (0.28, 1.21)	
Median confirmed DOR, months (95% CI)	NR (13.2, NE)	9.7 (4.6, NE)
HR (95% CI)	0.2 (0.07, 0.52)	

CI, confidence interval. DOR, duration of response. NE, not evaluable. NR, not reached. OS, overall survival. PFS, ORR, and DOR were based on IRRC assessments.
*The cutoff date for IRRC-assessed results was October 31, 2024.