Poster #440

HLX22 plus trastuzumab and XELOX for first-line treatment of HER2-positive locally advanced or metastatic gastric/gastroesophageal junction cancer (G/GEJC): updated results with additional patients

Jin Li[1,*], Ning Li[2], Mudan Yang[3], Yanqiao Zhang[4], Diansheng Zhong[5], Meng Qiu[6], Linzhi Lu[7], Xiaoming Hou[8], Yanru Qin[2], Guoping Sun[9], Jun Deng[10], Zimin Liu[11], Bo Liu[12], Yuntao Ma[13], Jingdong Zhang[14], Futang Yang[15], Haoyu Yu[15], Jing Li[15], Qingyu Wang[15], Jun Zhu[15], HLX22-GC Investigators

[1]Department of Oncology, Shanghai GoBroad Cancer Hospital, Shanghai, China; [2]Department of Medical Oncology, The Affiliated Cancer Hospital of Zhengzhou University & Henan Cancer Hospital, Zhengzhou, China; [3]Department of Gastroenterology, Shanxi Cancer Hospital, Taiyuan, China; [4]Department of Gastrointestinal Medical Oncology, Harbin Medical University Cancer Hospital, Harbin, China; [5]Department of Medical Oncology, Tianjin Medical University General Hospital, Tianjin, China; [6]Department of Abdominal Oncology, West China Hospital, West China School of Medicine, Sichuan University, Chengdu, China; [7]Department of Gastroenterology, Gansu Wuwei Tumour Hospital, Wuwei, China; [8]Department of Medical Oncology, The First Hospital of Lanzhou University, Lanzhou, China; [9]Department of Medical Oncology, The First Affiliated Hospital of Anhui Medical University, Hefei, China; [10]Department of Medical Oncology, The First Affiliated Hospital of Nanchang University, Nanchang, China; [11]Department of Oncology, Affiliated Hospital of Qingdao University, Qingdao, China; [12]Department of Gastroenterology, Shandong Provincial Cancer Hospital, Jinan, China; [13]Department of General Surgery, Gansu Provincial Hospital, Lanzhou, China; [14]Department of Internal Medicine, Liaoning Cancer Hospital, Shenyang, China; [15]Shanghai Henlius Biotech, Inc., Shanghai, China

Background

- Gastric/gastroesophageal junction cancer (G/GEJC) represents a major global healthcare burden. G/GEJC is often diagnosed at the advanced stage[2] and is associated with poor prognosis with a 5-year relative survival rate of approximately 6%[3].
- Around 12–23% of patients with gastric cancer have HER2-positive disease[2], for which trastuzumab plus chemotherapy is the recommended first-line therapy. However, survival outcomes remain unsatisfactory[4].
- The HLX22-GC201 study evaluates the efficacy and safety of HLX22 (a novel anti-HER2 antibody) combined with HLX02 (a trastuzumab biosimilar, hereafter referred as trastuzumab) and XELOX as first-line treatment for HER2-positive advanced G/GEJC (NCT04908813).
- Following our previous findings in 17-18 patients for each treatment group at the 2024 ASCO GI Cancers Symposium after a 14-month follow-up, here we report updated data with 31 additional patients after an extended follow-up.

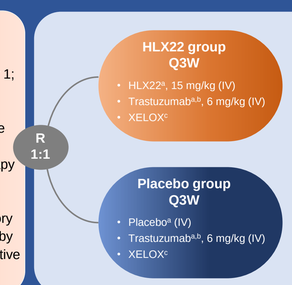
Methods

- Herein reported are results from Stage 2 of the study, in which patients with locally advanced or metastatic HER2-positive G/GEJC and no prior systemic antitumor therapy were randomized in a 1:1 ratio to HLX22 + trastuzumab + XELOX (HLX22 group) or placebo + trastuzumab + XELOX (placebo group) in 3-week cycles (**Figure 1**).

Figure 1. Study design

Key inclusion criteria

- Age 18–80 years; ECOG PS 0 or 1;
- Histologically confirmed locally advanced or metastatic G/GEJ adenocarcinoma that could not be cured by surgery;
- No prior systemic antitumor therapy for this advanced or metastatic disease;
- Confirmed by the central laboratory as HER2-positive (i.e., HER2 3+ by IHC or HER2 2+ by IHC and positive by FISH).



Primary endpoints:
PFS and ORR assessed by IRRC per RECIST v1.1

Secondary endpoints:

- PFS assessed by investigator
- ORR assessed by investigator
- Overall survival
- DOR
- Quality of life
- Safety
- Pharmacokinetics
- Immunogenicity

[a]Up to 2 years; [b]Initial loading dose of 8 mg/kg; [c]oxaliplatin IV Q3W D1 (up to 8 cycles) + capecitabine PO BID D1-14 (up to 2 years);
DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FISH, fluorescence in situ hybridization; G/GEJ, gastric/gastroesophageal junction; IHC, immunohistochemistry; IRRC, independent radiological review committee; IV, intravenous; ORR, objective response rate; PFS, progression-free survival; Q3W: every 3 weeks; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors.

Conclusions

- These efficacy and safety findings suggested that the addition of HLX22 to trastuzumab plus XELOX conferred survival benefit along with a manageable safety profile.
- Further investigation of HLX22 plus trastuzumab and XELOX as first-line treatment for HER2-positive advanced G/GEJC is warranted.

Results

- As of data cutoff on June 30, 2024, 62 patients were randomized to the HLX22 and placebo groups (n=31 each), all of whom were included in the efficacy and safety analyses.
- Median follow-up was 20.3 months for HLX22 group and 24.0 months for placebo group.
- Demographic and baseline clinical characteristics were generally balanced between the two groups. Median age was 60.0 and 64.0, respectively; 83.9% and 80.6% patients were male; 64.5% and 61.3% patients had ECOG PS 1; 96.8% patients had stage IV disease in both groups.
- More patient characteristics are detailed in **Table 1**.

Table 1. Patient demographics and baseline characteristics

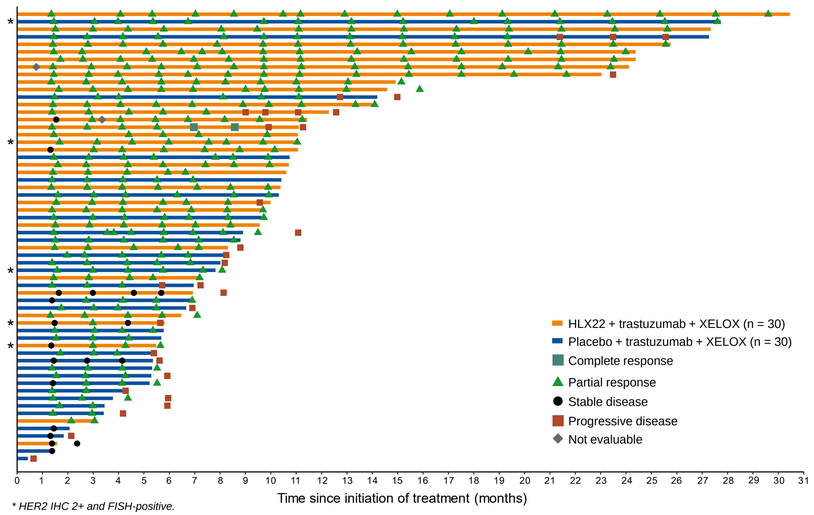
	HLX22 group (n = 31)	Placebo group (n = 31)
Median age (range), years	60.0 (26–78)	64.0 (28–74)
Male, n (%)	26 (83.9)	25 (80.6)
Median body mass index, kg/m^2 (range)	23.0 (16.8–29.4)	21.5 (17.5–27.5)
ECOG PS 1, n (%)	20 (64.5)	19 (61.3)
Median LVEF, % (range)	64.0 (57–74)	64.0 (60–71)
≥ 55%, n (%)	31 (100)	31 (100)
Primary tumor site, n (%)		
Gastric	22 (71.0)	23 (74.2)
GEJ	9 (29.0)	7 (22.6)
HER2 status[a], n (%)		
IHC 2+ and FISH-positive	3 (9.7)	2 (6.5)
IHC 3+	28 (90.3)	29 (93.5)
Histological subtype, n (%)		
Diffuse	1 (3.2)	2 (6.5)
Intestinal	6 (19.4)	4 (12.9)
Mixed or others	21 (67.7)	23 (74.2)
Stage IV disease, n (%)	30 (96.8)	30 (96.8)
Liver metastasis, n (%)	19 (61.3)	18 (58.1)
Lung metastasis, n (%)	5 (16.1)	6 (19.4)
Peritoneal metastasis, n (%)	4 (12.9)	5 (16.1)
Number of metastatic sites, n (%)		
1–2	24 (77.4)	23 (74.2)
> 2	6 (19.4)	7 (22.6)
Previous gastrectomy, n (%)	7 (22.6)	6 (19.4)
Previous chemotherapy, n (%)	4 (12.9)	2 (6.5)

[a]HER2 FISH testing was not required for patients with HER2 IHC 3+ tumors.
ECOG PS, Eastern Cooperative Oncology Group performance status; FISH, fluorescence in situ hybridization; IHC, immunohistochemistry; LVEF, left ventricular ejection fraction.

Efficacy

- IRRC-assessed confirmed ORR was 87.1% (95% confidence interval [CI] 70.2–96.4) for HLX22 group and 80.6% (62.5–92.5) for placebo group. Other major efficacy findings are detailed in **Table 2** and **Figures 2-4**.
- Median overall survival (95% CI) was not reached (17.6 months–not evaluable [NE]) for HLX22 group and 22.0 months (10.6 –NE) for placebo group (hazard ratio [95%], 0.5 [0.20–1.21]).
- Median progression-free survival (95% CI) was not reached (23.5 months–NE) and 8.3 months (5.7–12.7) for respective groups (hazard ratio [95% CI], 0.2 [0.06–0.45]).

Figure 2. Swimmer plot according to IRRC assessments per RECIST v1.1



** HER2 IHC 2+ and FISH-positive.*
Excluding two patients with no post-baseline tumor assessment.
FISH, fluorescence in situ hybridization; IHC, immunohistochemistry c; IRRC, independent radiological review committee; RECIST, Response Evaluation Criteria in Solid Tumors; XELOX, oxaliplatin+capecitabine.

Correspondence: Professor Jin Li; E-mail: lijin@csco.org.cn
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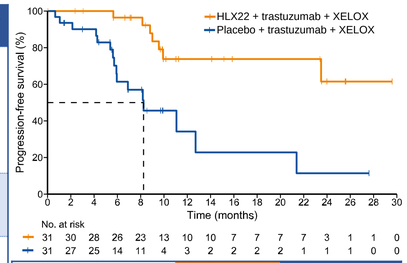
Table 2. Confirmed tumor response according to IRRC assessments and subsequent anti-HER2 therapy

	HLX22 group (n = 31)	Placebo group (n = 31)
Best overall response, n (%)		
Complete response	1 (3.2)	0
Partial response	26 (83.9)	25 (80.6)
Stable disease	3 (9.7)	3 (9.7)
Progressive disease	0	2 (6.5)
Not evaluable	1 (3.2)	1 (3.2)
ORR, % (95% CI)	87.1 (70.2–96.4)	80.6 (62.5–92.5)
Odds ratio (95% CI)	1.6 (0.4–6.5)	
ORR at Week 48 (95% CI)	38.7 (21.8–57.8)	9.7 (2.0–25.8)
Median DOR, month (95% CI)	NR (22.1–NE)	9.7 (4.6–20.0)
Hazard ratio (95% CI)	0.1 (0.04–0.41)	
12-month DOR rate (95% CI)	78.5 (51.8–91.4)	26.3 (5.1–55.0)
Subsequent anti-HER2 therapy, n (%)	3 (9.7)	13 (41.9)
Antibody-drug conjugate	3 (9.7)	8 (25.8)
Monospecific antibody	1 (3.2)	2 (6.5)
Bispecific antibody	0	3 (9.7)[a]

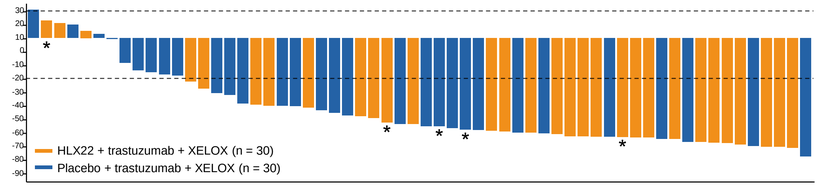
[a]Including one patient in a blinded trial.
CI, confidence interval; DOR, duration of response; IRRC, independent radiological review committee; NR, not reached; m, median; ORR, objective response rate; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; XELOX, oxaliplatin+capecitabine.

Figure 3. Kaplan–Meier curve of PFS according to IRRC assessments



	HLX22 group (n = 31)	Placebo group (n = 31)
mPFS, months (95% CI)	NR (23.5–NE)	8.3 (5.7–12.7)
HR (95% CI)	0.2 (0.06–0.45)	
12-month PFS rate (95% CI)	73.8 (50.3–87.4)	34.2 (12.0–58.1)
24-month PFS rate (95% CI)	61.5 (30.4–82.0)	11.4 (0.8–38.1)

Figure 4. Waterfall plot according to IRRC assessments per RECIST v1.1



** HER2 IHC 2+ and FISH-positive.*
Excluding two patients with no post-baseline tumor assessment.
FISH, fluorescence in situ hybridization; IHC, immunohistochemistry; IRRC, independent radiological review committee; RECIST, Response Evaluation Criteria in Solid Tumors; XELOX, oxaliplatin+capecitabine.

Safety

- Thirty (96.8%) and thirty-one (100%) patients experienced at least one treatment-emergent adverse event (TEAE) in respective groups (**Table 3**).
- Grade ≥ 3 treatment-emergent adverse events (TEAEs) were reported in 54.8% and 48.4% of the patients.
- More safety findings, including the most common TEAEs, are detailed in **Tables 3 and 4.**

Table 3. Summary of adverse events

	HLX22 group (n = 31)	Placebo group (n = 31)
Any TEAE	30 (96.8)	31 (100)
Grade ≥ 3	17 (54.8)	15 (48.4)
Leading to death	0	4 (12.9)
Leading to tx discontinuation	3 (9.7)	7 (22.6)
Any AESI	14 (45.2)	6 (19.4)
Infusion-related reaction	14 (45.2)	6 (19.4)
Related to HLX22/placebo	4 (12.9)	0
Cardiac-related	1 (3.2)	0
Any TRAE	30 (96.8)	30 (96.8)
Leading to death	0	1 (3.2)
Related to HLX22/placebo	27 (87.1)	14 (45.2)
Grade ≥ 3	9 (29.0)	6 (19.4)
Leading to tx discontinuation	2 (6.5)	2 (6.5)

Table 4. Most common TEAEs (≥ 25% in either group)

	HLX22 group (n = 31)	Placebo group (n = 31)
Platelet count decreased	25 (80.6)	23 (74.2)
Neutrophil count decreased	25 (80.6)	17 (54.8)
Anemia	18 (58.1)	19 (61.3)
White blood cell count decreased	18 (58.1)	18 (58.1)
Chills	14 (45.2)	4 (12.9)
Aspartate aminotransferase increased	13 (41.9)	6 (19.4)
Hypoesthesia	11 (35.5)	7 (22.6)
Vomiting	10 (32.3)	7 (22.6)
Pyrexia	10 (32.3)	5 (16.1)
Nausea	8 (25.8)	9 (29.0)
Hypokalemia	8 (25.8)	7 (22.6)
COVID-19	8 (25.8)	1 (3.2)
Hypoalbuminemia	6 (19.4)	9 (29.0)

AESI, Adverse event of special interest; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event; tx, treatment.

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