422P: HLX22 plus HLX02 and XELOX as first-line therapy for HER2-positive advanced gastric/gastroesophageal junction cancer: updated results from a randomized, double-blind phase 2 study

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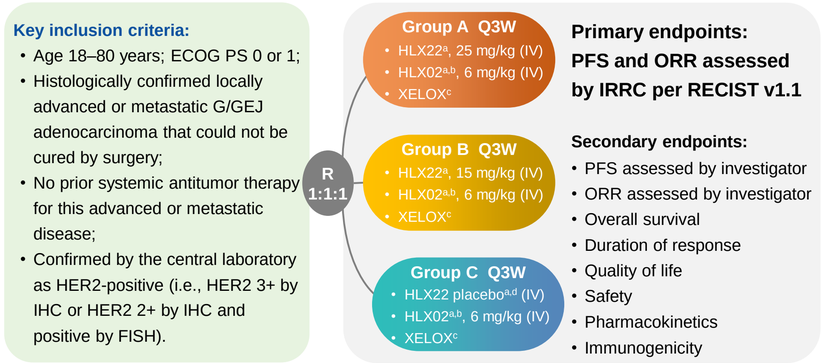
Background

- Gastric/gastroesophageal junction (G/GEJ) cancer represents a global healthcare challenge. It ranked fifth among all cancers, with nearly 1 million new cases estimated in 2022.[1]
- G/GEJ cancer is often diagnosed at the advanced stage.[2] The prognosis is poor with a 5-year relative survival rate of only 6%.[3] Around 12–23% of patients with gastric cancer have HER2-positive disease.[2] Although trastuzumab plus chemotherapy prolonged median overall survival in these patients, the improvement remains unsatisfactory.[4]
- At the 2024 ASCO Gastrointestinal Cancers Symposium, we reported results of first-line treatment with HLX22 (a novel anti-HER2 antibody) in combination with HLX02 (a trastuzumab biosimilar) and XELOX for HER2-positive advanced G/GEJ cancer (NCT04908813) with a median follow-up duration of 14.3 months. Here we report the updated efficacy and safety with another 7.8 months of follow-up.

Methods

- This ongoing phase 2 trial screened patients at 28 study sites in China. The study consisted of a single-arm safety run-in Stage 1, and a randomized Stage 2. Stage 2 was further divided into a double-blind part (Part 1) and an open-label part (Part 2). The present report focuses on Part 1 of Stage 2.
- In Part 1, patients were randomized 1:1:1 to receive different doses of HLX22 plus HLX02 and XELOX, or HLX22 placebo plus HLX02 and XELOX (Figure 1).
- Tumor imaging by computed tomography or magnetic resonance imaging was scheduled at screening, once every 6 weeks for 48 weeks from the first dose of study drugs, and every 9 weeks thereafter.

Figure 1. Study design



[a]*Up to 2 years;* [b]*Initial loading dose of 8 mg/kg;* [c]*IV oxaliplatin (up to 8 cycles) + oral capecitabine (up to 2 years);* [d]*Dose equivalent to HLX22 25 mg/kg. 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.*

Results

- As of 25 March 2024 (data cutoff), 82 patients were screened in Part 1; 53 patients were enrolled and randomized to group A (n=18), B (n=17), and C (n=18), and comprised the intention-to-treat population.
- The median follow-up duration was 22.1 months.
- The median age of all patients was 60.0 years. 44 (83.0%) patients were male. 30 (56.6%) patients had an ECOG PS score of 1. All patients had stage IV disease, and had distant metastases.
- Baseline demographics and characteristics of group A , B and C are shown in Table 1.

References

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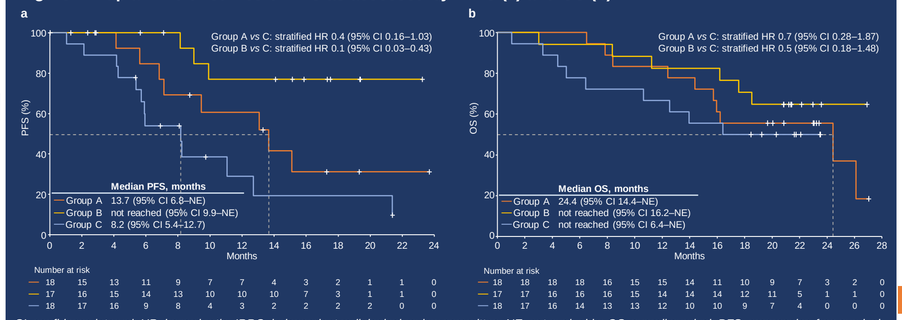
The prolonged PFS and enhanced antitumor response brought by the addition of HLX22 to HLX02 + XELOX as first-line therapy were achieved with manageable safety in patients with HER2-positive G/GEJ cancer.

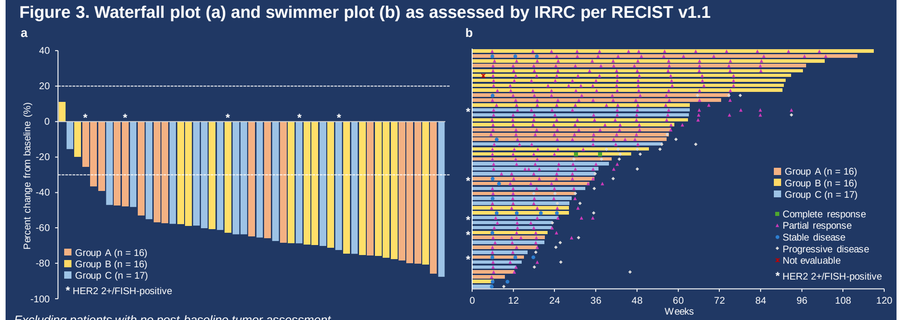
Efficacy

Figure 2. Kaplan–Meier curves of PFS as assessed by IRRC (a) and OS (b)



CI, confidence interval; HR, hazard ratio; IRRC, independent radiological review committee; NE, not evaluable; OS, overall survival; PFS, progression-free survival.

Figure 3. Waterfall plot (a) and swimmer plot (b) as assessed by IRRC per RECIST v1.1



Excluding patients with no post-baseline tumor assessment.
IRRC, independent radiological review committee; RECIST, Response Evaluation Criteria in Solid Tumors; FISH, fluorescence in situ hybridization.

Table 2. Tumor response[a] assessed by IRRC per RECIST v1.1 and subsequent therapy

	Group A (n = 18)	Group B (n = 17)	Group C (n = 18)
Complete response	0	1 (5.9)	0
Partial response	14 (77.8)	13 (76.5)	16 (88.9)
Stable disease	1 (5.6)	2 (11.8)	0
Progressive disease	0	0	1 (5.6)
NE	3 (16.7)	1 (5.9)	1 (5.6)
ORR, % (95% CI)	77.8 (52.4–93.6)	82.4 (56.6–96.2)	88.9 (65.3–98.6)
Odds ratio[b] (95% CI)	0.4 (0.07–2.73)	0.6 (0.09–4.32)	NA
ORR at week 36, % (95% CI)	44.4 (21.5–69.2)	64.7 (38.3–85.8)	27.8 (9.7–53.5)
ORR at week 75, % (95% CI)	16.7 (3.6–41.4)	41.2 (18.4–67.1)	5.6 (0.1–27.3)
Median DOR, month (95% CI)	11.8 (5.5–NE)	NR (8.6–NE)	6.8 (4.4–11.3)
Hazard ratio[b] (95% CI)	0.5 (0.19–1.34)	0.1 (0.02–0.41)	NA
Subsequent anti-HER2 therapy, n (%)	3 (16.7)	3 (17.6)	8 (44.4)
Antibody-drug conjugate	3 (16.7)	3 (17.6)	4 (22.2)
Monospecific antibody	0	1 (5.9)	1 (5.6)
Bispecific antibody	0	0	3 (16.7)[c]

[a]*Confirmed tumor response;* [b]*Odds ratio and hazard ratio were estimated between group A and C, as well as between group B and C;* [c]*One patient in blinded trial. CI, confidence interval; DOR, duration of response; IRRC, independent radiological review committee; NA, not applicable; NE, not evaluable; NR, not reached; ORR, objective response rate; RECIST, Response Evaluation Criteria in Solid Tumors.*

Table 1. Patient demographics and baseline characteristics

	Group A (n = 18)	Group B (n = 17)	Group C (n = 18)
Median age, years (range)	63.0 (49–74)	57.0 (26–71)	62.0 (28–72)
Male, n (%)	13 (72.2)	16 (94.1)	15 (83.3)
Median body mass index, kg/m^2 (range)	21.2 (17.6–27.8)	24.1 (19.0–29.4)	22.2 (18.6–27.5)
ECOG PS 1, n (%)	9 (50.0)	11 (64.7)	10 (55.6)
LVEF, median, % (range)	62.0 (58–69)	65.0 (56.5–74)	63.8 (61–71)
≥ 55%, n (%)	18 (100)	17 (100)	18 (100)
HER2 status[a], n (%)			
IHC 2+ and FISH-positive	2 (11.1)	1 (5.9)	2 (11.1)
IHC 3+	16 (88.9)	16 (94.1)	16 (88.9)
Tumor site, n (%)			
Gastric	17 (94.4)	13 (76.5)	14 (77.8)
Gastroesophageal junction	1 (5.6)	4 (23.5)	4 (22.2)
Stage IV disease, n (%)	18 (100)	17 (100)	18 (100)
Liver metastasis, n (%)	12 (66.7)	12 (70.6)	11 (61.1)
Number of metastatic sites, n (%)			
1–2	14 (77.8)	13 (76.5)	14 (77.8)
>2	4 (22.2)	4 (23.5)	4 (22.2)
Previous gastrectomy, n (%)	2 (11.1)	4 (23.5)	0
Previous chemotherapy, n (%)	2 (11.1)	1 (5.9)	0

[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.

Safety

- Summary of adverse events for group A, B, and C is provided in Table 3.
- HLX22 plus HLX02 and XELOX as first-line therapy was well tolerated in patients with HER2-positive advanced G/GEJ cancer.

Table 3. Summary of adverse events

n (%)	Group A (n = 18)		Group B (n = 17)		Group C (n = 18)	
Any TEAE	18 (100)		16 (94.1)		18 (100)	
Grade ≥3	15 (83.3)		8 (47.1)		8 (44.4)	
Grade 5	3 (16.7)		0		3 (16.7)	
Serious	10 (55.6)		5 (29.4)		5 (27.8)	
Leading to treatment discontinuation	4 (22.2)		1 (5.9)		3 (16.7)	
Any TRAE	18 (100)		16 (94.1)		17 (94.4)	
Grade 5	0		0		1 (5.6)	
Serious	6 (33.3)		1 (5.9)		1 (5.6)	
Related to HLX22/placebo	17 (94.4)		15 (88.2)		11 (61.1)	
Grade ≥3	10 (55.6)		3 (17.6)		3 (16.7)	
Leading to treatment discontinuation	1 (5.6)		1 (5.9)		1 (5.6)	
Adverse event of special interest	7 (38.9)		11 (64.7)		3 (16.7)	
Infusion-related reaction	7 (38.9)		11 (64.7)		3 (16.7)	
Related to HLX22/placebo	5 (27.8)		4 (23.5)		0	
Cardiac-related	1 (5.6)		1 (5.9)		0	
Most common TEAEs (≥40% in any group)	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3
Neutrophil count decreased	13 (72.2)	3 (16.7)	11 (64.7)	2 (11.8)	10 (55.6)	2 (11.1)
Anemia	13 (72.2)	3 (16.7)	10 (58.8)	2 (11.8)	13 (72.2)	0
White blood cell count decreased	13 (72.2)	4 (22.2)	9 (52.9)	0	11 (61.1)	1 (5.6)
Platelet count decreased	11 (61.1)	6 (33.3)	13 (76.5)	3 (17.6)	15 (83.3)	2 (11.1)
Aspartate aminotransferase increased	8 (44.4)	1 (5.6)	9 (52.9)	0	4 (22.2)	0
Chills	5 (27.8)	0	9 (52.9)	0	2 (11.1)	0
COVID-19	5 (27.8)	1 (5.6)	7 (41.2)	0	1 (5.6)	0
Hypoesthesia	3 (16.7)	0	7 (41.2)	0	4 (22.2)	0

TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

Acknowledgments and Disclosures

- The authors would like to acknowledge the participants in this study and their families, the investigators and staff at all clinical sites, and the members of the Independent Data Monitoring Committee.
- This study was funded by Shanghai Henlius Biotech, Inc. Editorial support was provided by Shiqi Zhong and Chen Hu from Shanghai Henlius Biotech, Inc.
- Futang Yang, Haoyu Yu, Jing Li, Alex Alika, Qingyu Wang, and Jun Zhu are employees of Shanghai Henlius Biotech, Inc.

ESMO Gastrointestinal Cancers Congress 2024, 26–29 June 2024