Abstract #4029: A phase 2 study of HLX07 as monotherapy or combination therapy in patients with locally advanced, unresectable, or metastatic esophageal squamous cell carcinoma

Jing Huang[1], Yun Liu[1], Tao Wu[2], Zhenyang Liu[3], Jin Zhou[4], Yuan Yuan[5], Mudan Yang[6], Bo Liu[7], Zhenbo Tan[8], Wu Zhuang[9], Jiayan Chen[10], Xuhui Hu[11], Xiaoli Hou[11], Haoyu Yu[11], Qingyu Wang[11], Jun Zhu[11]

[1]National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [2]Anyang Tumor Hospital, Anyang, China; [3]Hunan Cancer Hospital, the Affiliated Cancer Hospital of Xiangya School of Medicine, Central South University, Changsha, China; [4]Sichuan Cancer Hospital & Institute, Sichuan Cancer Center, Cancer Hospital Affiliated to School of Medicine, University of Electronic Science and Technology of China, Chengdu, China; [5]Xuzhou Central Hospital, Xuzhou, China; [6]Shanxi Cancer Hospital, Taiyuan, China; [7]Shandong Cancer Hospital & Institute, Shandong First Medical University and Shandong Academy of Medical Sciences, Jinan, China; [8]Xingtai People's Hospital, Xingtai, China; [9]Fujian Cancer Hospital, Fuzhou, China; [10]Fudan University Shanghai Cancer Center, Shanghai, China; [11]Shanghai Henlius Biotech, Inc., Shanghai, China

Background

- Esophageal cancer is one of the most common cancers worldwide, with esophageal squamous cell carcinoma (ESCC) accounting for about 84% of all esophageal cancer cases.[1] Most patients are diagnosed at the advanced stage, and the prognosis remains poor.[2,3]
- About 50–70% of ESCC cases showed overexpression of epidermal growth factor receptor (EGFR) which was related to shorter overall survival and disease-free survival, indicating that treatment targeting EGFR could be a promising strategy.[4–6]
- This study aimed to evaluate the efficacy and safety of HLX07, a novel recombinant humanized anti-EGFR monoclonal antibody, as monotherapy or combination therapy in patients with locally advanced, unresectable/metastatic ESCC.

Methods

- This was an open-label, multicenter, phase 2 study conducted at 10 hospitals in China (Figure 1).
- Patients with no prior systemic antitumor therapy were assigned to group A and given HLX07 1000 mg + serplulimab 200 mg (anti-PD-1 mAb) + 5-FU 2400 mg/m^2 + cisplatin 50 mg/m^2, Q2W IV.
- Patients who had failed first-line immuno-chemotherapy combination or at least two lines of other systemic antitumor therapy were assigned to group B and given HLX07 1000 mg, Q2W IV.
- Tumor imaging by computed tomography or magnetic resonance imaging was scheduled at baseline, every 6 weeks for 48 weeks from the first dose, and every 8 weeks thereafter. Tumor response was assessed by the IRRC and by investigators per RECIST v1.1.

Figure 1. Study design

Inclusion criteria:

- Age 18–75 years; ECOG PS 0 or 1
- Histologically or cytologically confirmed locally advanced, unresectable/metastatic ESCC or esophageal adenosquamous carcinoma
- No prior therapy with systemic anti-EGFR antibody
- Group A: no prior systemic antitumor therapy; Group B: failed first-line immuno-chemotherapy combination or ≥2 lines of other systemic antitumor therapy

Group A

- HLX07, 1000 mg
- Serplulimab[a], 200 mg
- Cisplatin[b], 50 mg/m^2
- 5-FU[c], 2400 mg/m^2

Q2W IV

Group B

HLX07, 1000 mg

Q2W IV

Primary endpoints:

ORR and PFS assessed by IRRC and investigators per RECIST v1.1

Secondary endpoints:

- DOR
- DCR
- TTR
- OS, 12-month OS rate
- 6- and 12-month PFS rate
- Safety
- Pharmacokinetics
- Immunogenicity
- Biomarker explorations
- Quality of life

[a] Up to 2 years (52 cycles); [b] Up to 8 cycles; [c] Up to 12 cycles.
DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ESCC, esophageal squamous cell carcinoma; IRRC, independent radiological review committee; IV, intravenous; mAb, monoclonal antibody; ORR, objective response rate; OS, overall survival; PD-1, programmed cell death protein 1; PFS, progression-free survival; Q2W: every 2 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; TTR, time to response.

Results

- As of February 4, 2023, 49 patients were enrolled in group A (n = 30) and group B (n = 19), with a median follow-up duration of 2.9 months.
- The median age of patients in group A and group B was 64.5 and 59.0 years, respectively. 14 (46.7%) patients in group A had PD-L1 combined positive score ≥10 tumors.

References

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Presenter: Professor Jing Huang; E-mail: huangjingwg@163.com

The encouraging antitumor activity and manageable safety profile support further development of HLX07 as a new treatment option for patients with advanced ESCC, both in first-line and late-line settings.

Efficacy

Table 2. Tumor response[a] in efficacy evaluable patients[b]

	Group A (n = 29)	Group B (n = 13)
ORR, % (95% CI)	**55.2** (35.7–73.6)	**23.1** (5.0–53.8)
DCR, % (95% CI)	**72.4** (52.8–87.3)	**38.5** (13.9–68.4)
CR, n (%)	0	0
PR, n (%)	16 (55.2)	3 (23.1)
SD, n (%)	5 (17.2)	2 (15.4)
PD, n (%)	4 (13.8)	6 (46.2)
NE, n (%)	4 (13.8)	2 (15.4)

- Among the 42 efficacy evaluable patients, median follow-up duration was 2.9 months in group A and 4.0 months in group B.
- Investigator-assessed ORRs were **55.2%** and **23.1%** in group A and group B, respectively.
- Investigator-assessed median PFS was not reached in group A; it was 1.5 months (95% CI 1.2–NE) in group B.

[a] Unconfirmed tumor response assessed by investigators per RECIST v1.1.
[b] Patients with at least one post-baseline tumor assessment or died.
CI, confidence interval; CR, complete response; DCR, disease control rate; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease.

Figure 2. Best percentage change from baseline in target lesion size assessed by investigators[c]

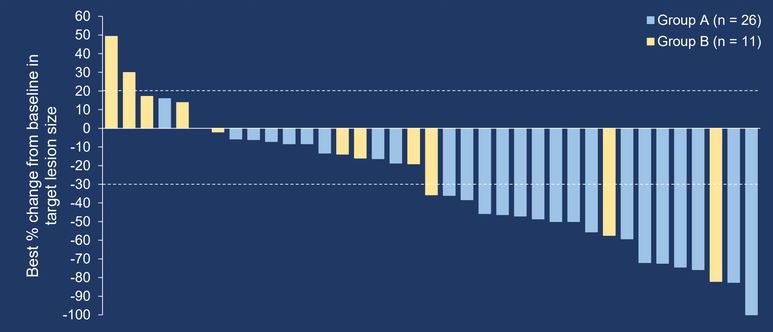
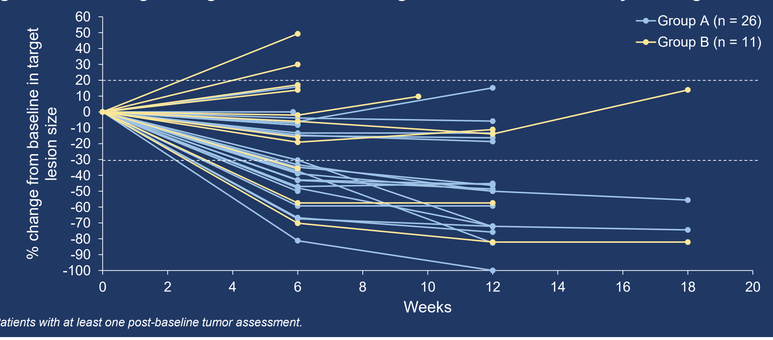


Figure 3. Percentage change from baseline in target lesion size assessed by investigators[c]



[c] Patients with at least one post-baseline tumor assessment.

- Baseline demographics and characteristics of group A and group B are shown in Table 1.

Table 1. Patient demographics and baseline characteristics

	Group A (n = 30)	Group B (n = 19)
Median age (range), years	64.5 (48–74)	59.0 (46–69)
Male, n (%)	26 (86.7)	19 (100.0)
ECOG PS, n (%)		
0	11 (36.7)	8 (42.1)
1	19 (63.3)	11 (57.9)
Disease status, n (%)		
Locally advanced	5 (16.7)	1 (5.3)
Distantly metastatic	25 (83.3)	18 (94.7)
Sites of metastases, n (%)		
Lymph node	20 (66.7)	15 (78.9)
Liver	8 (26.7)	4 (21.1)
Lung	3 (10.0)	2 (10.5)
Bone	2 (6.7)	2 (10.5)
Others	2 (6.7)	2 (10.5)
EGFR expression levels, n (%)		
H score ≥200	5 (16.7)	7 (36.8)
H score <200	24 (80.0)	12 (63.2)
Not available	1 (3.3)	0
Prior antitumor therapies, n (%)		
Chemotherapy	2 (6.7)[a]	19 (100.0)
Immunotherapy	0	18 (94.7)
Targeted therapy	0	7 (36.8)
Others	0	1 (5.3)[b]
Prior lines of therapy, n (%)		
1	0	4 (21.1)
2	0	10 (52.6)
3	0	3 (15.8)
4	0	2 (10.5)

[a] Adjuvant therapy; [b] Calcium Levofolinate.

Safety

- Most HLX07 related TRAEs were grade 1 or 2 (Table 3).
- AESIs were observed in 16 (53.3%) and 11 (57.9%) patients in group A and group B, respectively, most commonly rash and hypomagnesemia.
- There was no serious adverse event related to HLX07 or serplulimab. No treatment-related death was reported (Table 3).
- The most common TEAEs were rash, anemia, nausea, and hypomagnesemia (Table 4).

Table 3. Summary of TRAEs

n (%)	Group A (n = 30)	Group B (n = 19)
Any TRAEs	29 (96.7)	13 (68.4)
Related to serplulimab	17 (56.7)	0
Related to HLX07	25 (83.3)	13 (68.4)
Grade 1	13 (43.3)	6 (31.6)
Grade 2	6 (20.0)	5 (26.3)
Grade 3	6 (20.0)	1 (5.3)
Grade 4	0	1 (5.3)
Grade 5	0	0
Treatment interruption (HLX07 related)	5 (16.7)	0
Permanent treatment discontinuation (HLX07 related)	0	0
Serious	1 (3.3)[a]	0
Grade 5	0	0

Table 4. Most common TEAEs (≥15%)

n (%)	Group A (n = 30)	Group B (n = 19)
Anemia	18 (60.0)	2 (10.5)
Nausea	15 (50.0)	4 (21.1)
Rash	13 (43.3)	9 (47.4)
Hypomagnesemia	10 (33.3)	7 (36.8)
Hyponatremia	9 (30.0)	0 (0)
Vomiting	6 (20.0)	1 (5.3)
COVID-19	6 (20.0)	1 (5.3)
Decreased appetite	6 (20.0)	0 (0)
Sinus tachycardia	5 (16.7)	5 (26.3)
Platelet count decreased	5 (16.7)	2 (10.5)
Asthenia	5 (16.7)	2 (10.5)
Neutrophil count decreased	5 (16.7)	1 (5.3)
Lymphocyte count decreased	5 (16.7)	1 (5.3)
Hypercholesterolemia	5 (16.7)	0 (0)
Dry skin	2 (6.7)	3 (15.8)

[a] Related to chemotherapy.
AESI, adverse event of special interest; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

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