Abstract 759P: Efficacy and Safety of HLX07 Monotherapy in Advanced Cutaneous Squamous Cell Carcinoma: an Open-label, Multicenter Phase 2 Study

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Background

- Cutaneous squamous cell carcinoma (CSCC) accounts for 20% of all cutaneous cancers.[1] There were 2.4 million new CSCC cases in 2020, and incidence is projected to continue increasing.[2] Prognosis is poor for patients with metastatic CSCC; 10-year survival rate is <20% for patients with nodal metastasis and <10% for those with distant metastasis.[1,3] Moreover, 8% to 58% patients develop locoregional or metastatic recurrence depending on the risk factor profile[4].
- About 70% of CSCC cases showed overexpression of epidermal growth factor receptor (EGFR) which was related to poor prognosis, suggested targeting EGFR as a promising therapeutic strategy[5]. Available evidence showed objective response rate (ORR) of ~26% in a meta-analysis and 27.8% in a phase 2 trial of cetuximab and 31.2% in a phase 2 trial of panitumumab [6,7,8].
- HLX07 is a novel, fully-humanized anti-EGFR monoclonal antibody that has demonstrated promising anti-tumor efficacy and safety in phase I clinical trials[9,10].

Methods

- This open-label, multicenter phase 2 study is comprised of two parts. Part 1 investigates the preliminary efficacy of HLX07. Part 2 will assess the efficacy and safety of HLX07 in a larger cohort based on the fixed dosage established in part 1. Here, we will focus on updating the results from part 1. The study design of part 1 is presented below (Figure 1).
- 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 9 weeks thereafter. Tumor response was assessed by the IRRC and by investigators per RECIST v1.1.

Figure 1. Study design

Inclusion criteria:

- Age ≥18 years; ECOG PS 0 or 1
- Histologically or cytologically confirmed locally advanced, inoperable or not suited for curative radiotherapy/metastatic CSCC
- At least one measurable target lesion assessed by IRRC per RECIST v1.1 within 4 weeks prior to the first dose of study treatment
- Life expectancy of at least 12 weeks
- Adequate organ function

Group A
HLX07[a], 1500 mg
Q3W IV

Group B
HLX07[a], 1000 mg
Q3W IV

Primary endpoint:
ORR assessed by IRRC per RECIST v1.1

Secondary endpoints:

- ORR assessed by investigator
- DOR
- DCR
- TTR
- PFS, 6-and 12-month PFS rate
- OS, 12-month OS rate
- Safety
- Pharmacokinetics
- Immunogenicity
- Quality of life

[a] until loss of clinical benefit, disease progression, intolerable toxicity, withdrawal of inform consent, initiation of new antitumour therapy, or death (whichever occurred first)

CSCC, cutaneous squamous cell carcinoma; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IRRC, independent radiological review committee; IV, intravenous; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q3W: every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; TTR, time to response.

Results

- As of data cut-off on April 30, 2024, 31 patients were enrolled in group A (n = 21) and group B (n = 10) in part 1, with median follow-up duration of 19.1 months and 12.7 months, respectively.
- Overall, the median age was 60.0 years, and 16 (51.6%) patients were male; 12 patients had prior treatment with immunotherapy. More patient characteristics are shown in Table 1.

Table 1. Patient characteristics

	Group A (n = 21)	Group B (n = 10)
Median age (range), years	60.0 (32–97)	59.5 (41–82)
Male, n (%)	12 (57.1)	4 (40.0)
ECOG PS, n (%)		
0	4 (19.0)	3 (30.0)
1	16 (76.2)	7 (70.0)
Had nodal or distant metastasis, n (%)	18 (85.7)	9 (90.0)
Primary tumor site, n (%)		
Extremities	11 (52.4)	8 (80.0)
Head, face and neck	7 (33.3)	1 (10.0)
Anus and genitalia	2 (9.5)	1 (10.0)
Trunk	1 (4.8)	0
Had prior anti-cancer surgery, n (%)	15 (71.4%)	7 (70.0 %)
EGFR expression levels, n (%)		
H-score ≥150	6 (28.6)	7 (70.0)
H-score <150	14 (66.7)	3 (30.0)
Type of prior anti-cancer systemic therapy, n (%)	7 (33.3)	6 (60.0)
Chemotherapy	6 (28.6)	6 (60.0)
Immunotherapy	5 (23.8)	6 (60.0)
Targeted Therapy	1 (4.8)	1 (10.0)
Had prior anti-cancer systemic therapy, n (%)		
Neo-adjuvant	0	1 (10.0)
Adjuvant	1 (4.8)	1 (10.0)
First-line	4 (19.0)	1 (10.0)
Second-line	1 (4.8)	2 (20.0)
Third-line	1 (4.8)	1 (10.0)

Efficacy

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

	Group A (n = 21)	Group B (n = 10)
ORR, % (95% CI)	**19.0** (5.5–41.9)	**60.0** (26.2–87.8)
DCR, % (95% CI)	**61.9** (38.4–81.9)	**100.0** (69.2–100.0)
CR, n (%)	0	1 (10.0)
PR, n (%)	4 (19.0)	5 (50.0)
SD, n (%)	9 (42.9)	4 (40.0)
PD, n (%)	5 (23.8)	0
NE, n (%)	3 (14.3)	0

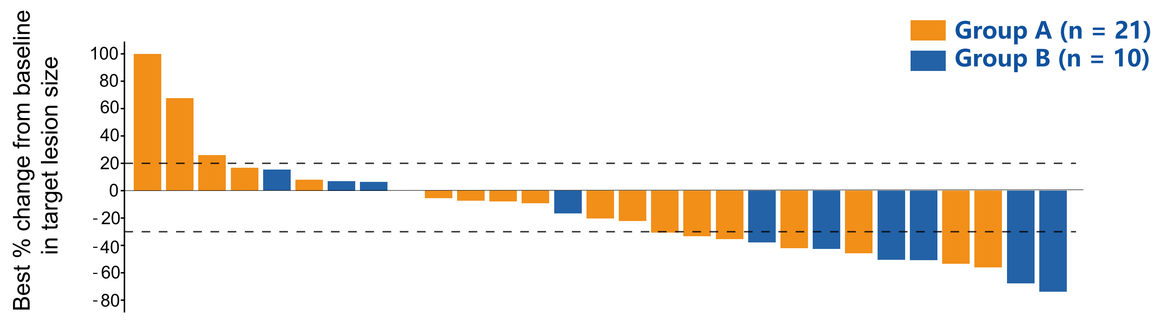
[a] Confirmed tumor response assessed by IRRC per RECIST v1.1.

[b] Patients with at least one post-baseline tumor assessment or died.

CI, confidence interval; CR, complete response; CSCC, cutaneous squamous cell carcinoma; DCR, disease control rate; DOR, duration of response; NE, not evaluable; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; IRRC, independent radiological review committee; SD, stable disease.

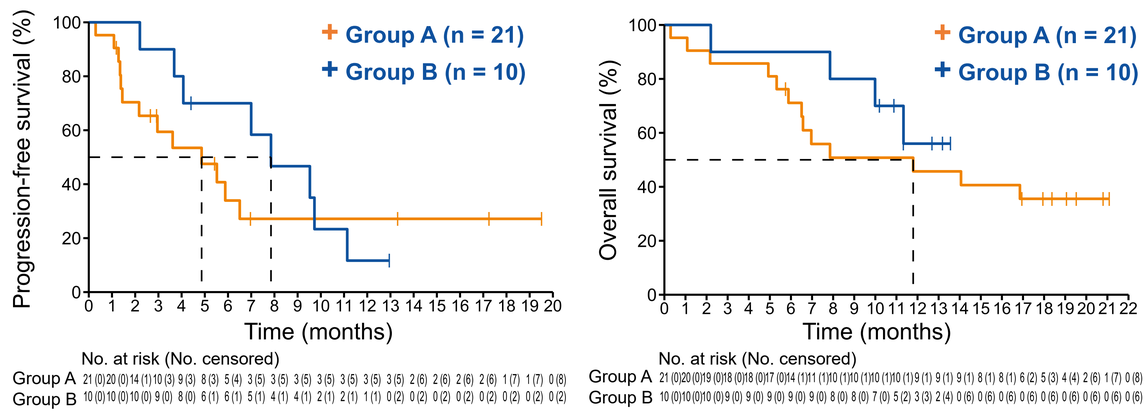
- IRRC-assessed confirmed ORRs were **19.0%** and **60.0%** for groups A and B, respectively (Table 2, Figure 2).
- IRRC-assessed confirmed DORs were 5.0 months (95% CI 2.9–16.8) for group A and 7.4 months (95% CI 2.8–not evaluable) for group B.
- IRRC-assessed median PFS was 4.9 months (95% CI 1.4–6.5) for group A and 7.9 months (95% CI 2.2–11.1) for group B (Figure 3, left panel).
- Median OS was 11.8 months (95% CI 5.9–not evaluable) for group A and not reached for group B (Figure 3, right panel).

Figure 2. Best percentage change from baseline in target lesion size assessed by IRRC*



** Two patients in group A had no tumor assessment before they died.*

Figure 3. Efficacy analysis, progression free survival and overall survival



Safety

- 13 (61.9%) patients in group A and 4 (40.0%) patients in group B reported at least one grade ≥3 treatment-emergent adverse events (TEAEs; Table 3).
- Most treatment-related adverse events (TRAEs) and adverse event of special interest (AESIs) were grade 1 or 2 (Table 3).
- No TRAE leading to HLX07 discontinuation or death was reported (Tables 3 and 4).
- The most common grade ≥3 TRAEs (≥5% in either group) were hypomagnesemia (group A, 14.3%; group B, 20.0%), rash (9.5%; 10.0%), and hypocalcemia (4.8%; 10.0%; Table 4).

Table 3. Safety summary

n (%)	Group A (n = 21)	Group B (n = 10)
Any TEAEs	21 (100.0)	10 (100.0)
Grade ≥3	13 (61.9)	4 (40.0)
Leading to HLX07 discontinuation	1 (4.8)	1 (10.0)
Leading to death	3 (14.3)	0
Serious TEAEs	9 (42.9)	2 (20.0)
Grade ≥3	8 (38.1)	1 (10.0)
Any TRAEs	18 (85.7)	10 (100.0)
Grade ≥3	8 (38.1)	3 (30.0)
Leading to HLX07 discontinuation	0	0
Leading to death	0	0
Any AESIs	13 (61.9)	9 (90.0)
Grade ≥3	5 (23.8)	3 (30.0)
Treatment-related	13 (61.9)	8 (80.0)
Serious	2 (9.5)	0

Table 4. Most common grade ≥3 adverse events

n (%)	Group A (n = 21)	Group B (n = 10)
Grade ≥3 TEAEs (≥5%), n (%)		
Hypomagnesemia	3 (14.3)	2 (20.0)
Death*	3 (14.3)	0
Rash	2 (9.5)	1 (10.0)
Hypokalemia	2 (9.5)	0
Grade ≥3 TRAEs, n (%)		
Hypomagnesemia	3 (14.3)	2 (20.0)
Rash	2 (9.5)	1 (10.0)
Hypocalcemia	1 (4.8)	1 (10.0)
Blood pressure increased	1 (4.8)	0
Hypokalaemia	1 (4.8)	0
Platelet count decreased	1 (4.8)	0
Pneumonia	1 (4.8)	0
Skin infection	1 (4.8)	0

** Cause of death unknown. Not related to HLX07 as assessed by the investigator.*

The promising efficacy and favorable safety results of HLX07 observed in patients with advanced CSCC warrant further investigation of HLX07 in larger scale clinical studies.

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