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First-line HLX07 plus serplulimab with chemotherapy in squamous non-small cell lung cancer: a phase 2 study

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INTRODUCTION

- Immunotherapy (PD-L1/PD-1 inhibitors) combined with chemotherapy has demonstrated efficacy and been approved as first-line treatment for advanced squamous non-small cell lung cancer (NSCLC)[1,2]. However, the prognosis remains unsatisfactory.
- Epidermal growth factor receptor (EGFR) is often overexpressed in advanced NSCLC[3,4], suggesting the potential of targeting this pathway in this disease indication.
- This randomized, multicenter phase 2 study evaluated the efficacy and safety of HLX07, a novel humanized anti-EGFR monoclonal antibody, plus serplulimab (anti-PD-1 antibody) and chemotherapy as first-line treatment for advanced squamous NSCLC.
- Previous analysis presented at the 2025 ASCO Annual Meeting showed encouraging efficacy of the tri-combination regimen. Here we report an updated analysis of the efficacy and safety findings.

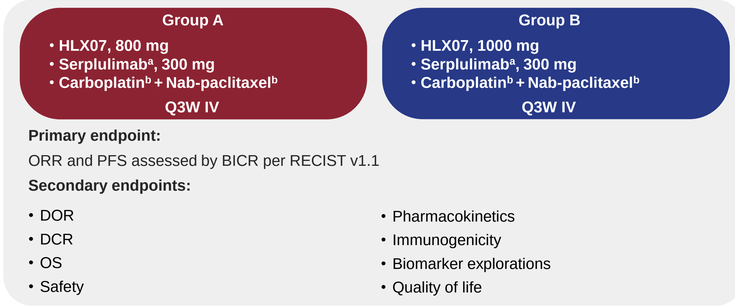
METHODS

- This phase 2 study assessed the combinations of HLX07 (at different doses), serplulimab, and chemotherapy.
- The study design is presented in **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 blinded independent central review and by investigators per RECIST v1.1.

Key inclusion criteria:

- Age ≥18 years; ECOG PS 0 or 1;
- Histologically confirmed stage IIIB/IIIC or IV (AJCC 8th edition) squamous NSCLC that could not be treated with surgery or radiation therapy;
- No prior systemic therapy for locally advanced or recurrent/metastatic squamous NSCLC;
- Provision of tumor tissue for determination of EGFR and PD-L1 expression levels; EGFR H-score ≥150 as confirmed by central laboratory;
- At least one measurable target lesion assessed by investigator per RECIST v1.1 within 4 weeks prior to the first dose of study treatment.

Figure 1. Study design



[a] *Up to 2 years;* [b] *4–6 cycles. Carboplatin: area under curve 5 (maximum dosage 750 mg) or area under curve 6 (maximum dosage 900 mg). Nab-paclitaxel: 260 mg/m². AJCC, American Joint Committee on Cancer; BICR, blinded independent central review; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; ORR, objective response rate; OS, overall survival; PD-L1, programmed cell death 1-ligand 1; PD-1, programmed cell death 1; PFS, progression-free survival; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors.*

RESULTS

- As of the data cut-off date of March 05, 2025, the median follow-up duration was 18.6 months.
- 27 patients were enrolled and randomly assigned to group A (n=13) and group B (n=14). All patients received at least one dose of study treatment and were included in the efficacy and safety analyses.
- 10 (76.9%) patients, and 11 (78.6%) patients had an ECOG PS of 1 in group A, and B, respectively (**Table 1**). More baseline demographics and characteristics are shown in **Table 1**.
- BICR-assessed ORRs were **69.2%** and **71.4%** in group A and group B, respectively (**Table 2**). BICR-assessed DCRs were 92.3% for group A, and 100.0% for group B (**Table 2**).
- Median PFS was not reached in group A and 17.4 months in group B (**Figure 2**). Median DOR and OS were not reached in either group.
- Confirmed responses of the patients over time are shown in **Figure 3**.
- Summary of adverse events is presented in **Table 3**. irAEs occurred in 6 (46.2%) patients in group A and 8 (57.1%) patients in group B. The most common ≥ grade 3 TEAEs are listed in **Table 4**.

Table 1. Patient demographics and baseline characteristics

	Group A (n = 13)	Group B (n = 14)
Median age (range), years	65 (54–80)	66 (50–72)
Sex, n (%)		
Male	11 (84.6)	12 (85.7)
Female	2 (15.4)	2 (14.3)
ECOG PS, n (%)		
0	3 (23.1)	3 (21.4)
1	10 (76.9)	11 (78.6)
Tumor stage, n (%)		
IIIB/C	5 (38.5)	7 (50.0)
IV	8 (61.5)	7 (50.0)
Site of metastases, n (%)		
Bone	2 (15.4)	1 (7.1)
Brain	0	1 (7.1)
Liver	1 (7.1)	0
PD-L1 expression*, TPS, n (%)		
TPS < 1%	8 (61.5)	6 (42.9)
1% ≤ TPS < 50%	3 (23.1)	5 (35.7)
TPS ≥ 50%	2 (15.4)	3 (21.4)
EGFR expression, H-score		
H-score < 200, n (%)	7 (53.8)	7 (50.0)
H-score ≥ 200, n (%)	6 (46.2)	7 (50.0)
Median	190.0	202.5
Range	150–275	155–290

Table 2. Tumor response[a]

	Group A (n = 13)	Group B (n = 14)
ORR, % (95% CI)	**69.2** (38.6–90.9)	**71.4** (41.9–91.6)
DCR, % (95% CI)	**92.3** (64.0–99.8)	**100.0** (76.8–100.0)
Complete response, n (%)	0	0
Partial response, n (%)	9 (69.2)	10 (71.4)
Stable disease, n (%)	3 (23.1)	4 (28.6)
Progressive disease, n (%)	1 (7.7)	0
Not evaluable, n (%)	0	0

Figure 2. BICR-assessed PFS per RECIST v1.1

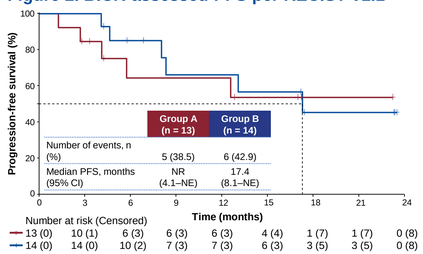
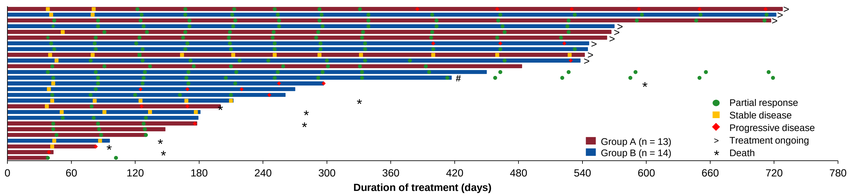


Figure 3. Swimmer plot of patients' confirmed tumor response as assessed by the BICR



* *Detected with 22C3.* [a] *Confirmed tumor response assessed by the BICR per RECIST v1.1. BICR, blinded independent central review; CI, confidence interval; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; irAE, immune-related adverse event; NE, not evaluable; NR, not reached; ORR, objective response rate; OS, overall survival; PD-L1, programmed cell death 1-ligand 1; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; TEAE, treatment-emergent adverse event. TPS, tumor proportion score.*

Table 3. Safety summary

n (%)	Group A (n = 13)	Group B (n = 14)
Any TEAEs	13 (100.0)	14 (100.0)
≥ Grade 3	13 (100.0)	13 (92.9)
Grade 3	6 (46.2)	11 (78.6)
Grade 4	6 (46.2)	2 (14.3)
Grade 5	1 (7.7)[a]	0
Leading to HLX07 or serplulimab discontinuation	3 (23.1)[b]	3 (21.4)[c]
Any TRAEs	13 (100.0)	14 (100.0)
HLX07 or serplulimab-related	13 (100.0)	14 (100.0)
≥ Grade 3	12 (92.3)	10 (71.4)
Grade 3	7 (53.8)	9 (64.3)
Grade 4	4 (30.8)[d]	1 (7.1)[e]
Grade 5	1 (7.7)[a]	0
Any AESIs	12 (92.3)	14 (100.0)
IRR	1 (7.7)	2 (14.3)
irAE	6 (46.2)	8 (57.1)
Rash (HLX07-related)	6 (46.2)	8 (57.1)
Hypomagnesemia (HLX07-related)	6 (46.2)	6 (42.9)
Serious	1 (7.7)	2 (14.3)

Table 4. Most common ≥ Grade 3 TEAEs

n (%)	Group A (n = 13)	Group B (n = 14)
≥ 10% in either group		
Neutrophil count decreased	7 (53.8)	9 (64.3)
White blood cell count decreased	7 (53.8)	5 (35.7)
Platelet count decreased	4 (30.8)	5 (35.7)
Anemia	4 (30.8)	3 (21.4)
Pneumonia	4 (30.8)	3 (21.4)
Hypokalemia	2 (15.4)	5 (35.7)
Hypomagnesemia	2 (15.4)	2 (14.3)
Hypocalcemia	2 (15.4)	1 (7.1)
Dermatitis acneiform	1 (7.7)	2 (14.3)
Lymphocyte count decreased	1 (7.7)	2 (14.3)
Rash	1 (7.7)	2 (14.3)

[a] *The patient with brain metastasis had a partial response at the first tumor assessment (with disappearance of the brain metastases) and a duration of response of over 21 months.* [a] *Death related to both HLX07 and serplulimab with preferred term of pneumonia.* [b] *Discontinuation of HLX07 and serplulimab occurred for two patients: one with pneumonia (grade 5) and one with hemoptysis (grade 2); discontinuation of serplulimab occurred for another patient with dermatitis and cellulitis (both grade 3).* [c] *Discontinuation of HLX07 and serplulimab occurred for two patients: one palmar-plantar erythrodysesthesia syndrome (grade 3) and one with supraventricular extrasystoles (grade 2); discontinuation of serplulimab occurred for another patient with sicca syndrome (grade 3).* [d] Two patients with TRAEs related to both HLX07 and serplulimab with preferred term of platelet count decreased, and neutrophil count decreased, respectively; one patient with TRAE related to HLX07 with preferred term of hypomagnesemia; one patient with TRAE related to serplulimab with preferred term of neutrophil count decreased. [e] related to HLX07 but not serplulimab. *AESI, adverse event of special interest; BICR, blinded independent central review; irAE, immune-related adverse event; IRR, infusion-related reactions; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.*

DISCUSSION AND CONCLUSION

Take Away Message

HLX07 in combination with serplulimab and chemotherapy conferred encouraging antitumor activity and manageable safety profile in patients with advanced squamous NSCLC.

Future Direction for Research

This tri-combination regimen warrants further investigation as a potential first-line treatment option for advanced squamous NSCLC.

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