Abstract 542P: First-line HLX07 Plus Serplulimab With or Without Chemotherapy Versus Serplulimab Plus Chemotherapy in Advanced/Recurrent Squamous Non-small Cell Lung Cancer: a Phase 2 study

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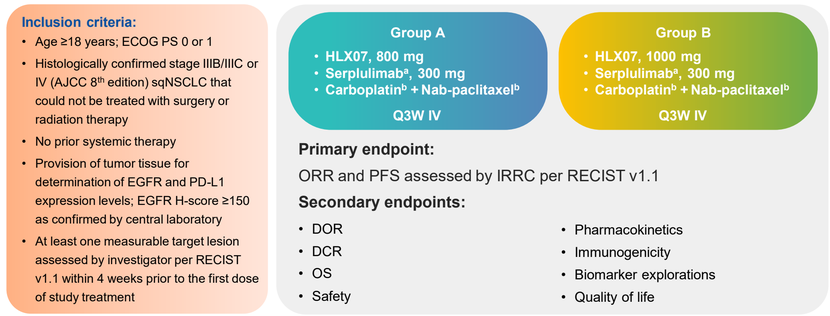
Background

- Lung cancer is the leading cause of cancer death worldwide[1], with squamous non-small cell lung cancer (sqNSCLC) accounting for 25-30% of all lung cancer cases.[2-4]
- Adding immunotherapy (PD-L1/PD-1 inhibitors) to chemotherapy has demonstrated efficacy and been approved for advanced sqNSCLC as first-line therapy.[5] However, the prognosis remains unsatisfactory.
- High expression of the epidermal growth factor receptor (EGFR) is prevalent in advanced NSCLC.[6]
- This study aimed to compare the efficacy of HLX07, a novel recombinant humanised anti-EGFR monoclonal antibody, plus serplulimab (anti-PD-1 antibody) ± chemotherapy versus serplulimab plus chemotherapy as first-line treatment for advanced sqNSCLC.

Methods

- This randomised, multicentre phase 2 study consisted of 4 parts and assessed different combinations of HLX07 (at various doses), serplulimab, and chemotherapy.
- Part 3 explored the preliminary efficacy of the three-drug combination and is presented in this report.
- 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



[a] Up to 2 years (52 cycles); [b] Up to 6 cycles

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.

Results

- As of the data cut-off date June 27, 2023, 12 patients were enrolled and randomly assigned to group A (n=6) and group B (n=6) in part 3 of the study.
- All patients received at least one dose of the intended combinatory drug treatments and were included in the intent-to-treat (ITT) population.
- 2 (33.3%) patients, and 4 (66.7%) patients had an ECOG PS of 0, and 1, respectively in each group (Table 1).

References

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The encouraging antitumor activity and manageable safety profile support further development of HLX07 plus serplulimab and chemotherapy as a new first-line treatment option for patients with advanced sqNSCLC.

Efficacy

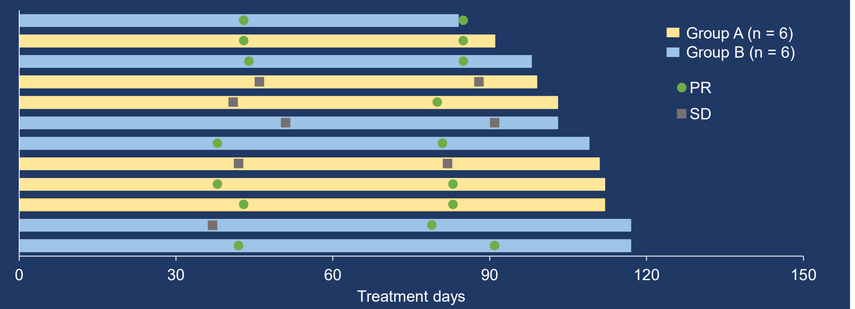
Table 2. Tumor response[a] in the ITT population

	Group A (n = 6)	Group B (n = 6)
ORR, % (95% CI)	**83.3** (35.9–99.6)	**66.7** (22.3–95.7)
DCR, % (95% CI)	**100.0** (54.1–100.0)	**100.0** (54.1–100.0)
CR, n (%)	0	0
PR, n (%)	5 (83.3)	4 (66.7)
SD, n (%)	1 (16.7)	2 (33.3)
PD, n (%)	0	0
NE, n (%)	0	0

- Median follow-up duration was 3.5 months for group A, and 3.6 months for group B.
- Investigator-assessed ORRs were **83.3%** and **66.7%** in group A and group B, respectively.
- Investigator-assessed DCRs were 100.0% in both groups A, and group B.
- Median PFS and OS was not reached in either groups.

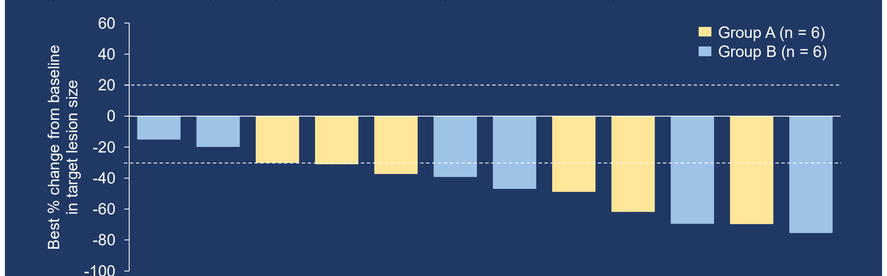
[a] Unconfirmed tumor response assessed by investigator per RECIST v1.1. CI, confidence interval; CR, complete response; DCR, disease control rate; ITT, intent-to-treat; NE, not evaluable; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease.

Figure 2. Swimmer plot of patients' tumor response (investigator-assessed per RECIST v1.1)



PR, partial response; SD, stable disease

Figure 3. Best percentage change from baseline in target lesion size (investigator-assessed[b])



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

- More baseline demographics and characteristics of patients in group A and group B are shown in Table 1.

Table 1. Patient demographics and baseline characteristics

	Group A (n = 6)	Group B (n = 6)
Median age (range), years	61.5 (55–80)	64.5 (50–69)
Male, n (%)	5 (83.3)	6 (100.0)
ECOG PS, n (%)		
0	2 (33.3)	2 (33.3)
1	4 (66.7)	4 (66.7)
Squamous NSCLC type, n (%)		
Locally advanced	2 (33.3)	1 (16.7)
Distant metastasis	4 (66.7)	5 (83.3)
Tumor stage, n (%)		
IIIB	1 (16.7)	0
IIIC	0	1 (16.7)
IVA	4 (66.7)	4 (66.7)
IVB	1 (16.7)	1 (16.7)
PD-L1 expression, TPS, n (%)		
TPS < 1%	5 (83.3)	3 (50.0)
1% ≤ TPS < 50%	1 (16.7)	2 (33.3)
TPS ≥ 50%	0	1 (16.7)
EGFR expression, H-score		
Median	195.0	192.5
Range	150–230	155–260
ALK fusion positive, n (%)		
Yes	0	0
No	0	1 (16.7)

Safety

- 2 (33.3%) patients in group A and 3 (50.0%) patients in group B reported HLX07-related grade ≥3 TEAEs; 2 (33.3%) patients in group A and 2 (33.3%) patients in group B reported serplulimab-related grade ≥3 TEAEs (Table 3).
- There were no TRAEs leading to death. AESIs occurred in 5 (83.3%) patients in group A and all patients in group B.
- The most common TRAEs (≥ 3 patients) are listed in Table 4.

Table 3. Safety summary

n (%)	Group A (n = 6)	Group B (n = 6)
Any TEAEs	6 (100.0)	6 (100.0)
≥Grade 3	2 (33.3)	5 (83.3)
Leading to treatment discontinuation	1 (16.7)	0
Leading to death	0	0
Any TRAEs	6 (100.0)	6 (100.0)
HLX07-related	6 (100.0)	6 (100.0)
≥Grade 3	2 (33.3)	3 (50.0)
Serplulimab-related	6 (100.0)	4 (66.7)
≥Grade 3	2 (33.3)	2 (33.3)
Any AESIs	5 (83.3)	6 (100.0)
IRR	0	0
irAE	0	0
Rash (HLX07-related)	3 (50.0)	2 (33.3)
Hypomagnesemia (HLX07-related)	1 (16.7)	1 (16.7)
Serious	0	0

Table 4. Most common TRAEs (≥ 3 patients)

n (%)	Group A (n = 6)	Group B (n = 6)
TRAEs (≥ 3 patients), n (%)		
Related to HLX07		
White blood cell count decreased	4 (66.7)	1 (16.7)
Neutrophil count decreased	4 (66.7)	1 (16.7)
Anaemia	4 (66.7)	0
Rash	3 (50.0)	2 (33.3)
Alopecia	3 (50.0)	2 (33.3)
Decreased appetite	3 (50.0)	1 (16.7)
Platelet count decreased	3 (50.0)	1 (16.7)
Related to serplulimab		
White blood cell count decreased	4 (66.7)	1 (16.7)
Neutrophil count decreased	4 (66.7)	1 (16.7)
Anaemia	4 (66.7)	0
Alopecia	3 (50.0)	2 (33.3)
Decreased appetite	3 (50.0)	1 (16.7)
Platelet count decreased	3 (50.0)	1 (16.7)
Rash	3 (50.0)	1 (16.7)

AESI, adverse event of special interest; irAE, immune-related adverse event; IRR, infusion-related reactions; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

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