Abstract 80P: Safety, preliminary efficacy, and pharmacokinetics of HLX26 plus serplulimab in advanced solid tumours: an open-label, dose-escalation phase 1 study

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Background

- Despite the compelling antitumour activity of anti-programmed cell death-1 (PD-1)/programmed cell death ligand 1 (PD-L1) agents, many patients will develop resistance to these therapies.[1]
- Recent study has demonstrated that adaptive resistance to PD-1/PD-L1 blockade may be associated with upregulation of alternative immune checkpoints, including lymphocyte activation gene-3 (LAG-3).[2]
- HLX26 is a novel humanised IgG4 monoclonal antibody targeting LAG-3. Serplulimab is a novel humanised IgG4 monoclonal antibody against the PD-1 receptor.
- This study aimed to evaluate the safety, preliminary efficacy, and pharmacokinetics of HLX26 plus serplulimab in patients with advanced solid tumours.

Methods

- This was a single-centre, open-label, dose-escalation phase 1 study conducted in China.
- Patients with histologically or cytologically confirmed advanced/metastatic solid tumours that had failed or could not receive standard therapies were enrolled and received intravenous HLX26 at three dose levels (500, 800, 1600 mg) together with serplulimab (300 mg) Q3W, following a “3+3” design (Figure 1).
- Tumour imaging by computed tomography or magnetic resonance imaging was scheduled at baseline, every 6 weeks for 48 weeks from the first dose, and every 12 weeks thereafter until disease progression, initiation of new antitumour treatment, death, or end of study, whichever occurred first. Tumour response was assessed by investigators per RECIST v1.1.

Figure 1. Study design

Inclusion criteria:
- Age 18–75 years
- ECOG PS 0 or 1
- Expected survival ≥3 months
- Histologically or cytologically confirmed advanced/metastatic solid tumours that had failed or could not receive standard therapies
- No prior therapy with anti-LAG-3 antibody
- At least one measurable lesion per RECIST v1.1

“3+3” Design

HLX26 500 mg Serplulimab 300 mg → HLX26 800 mg Serplulimab 300 mg → HLX26 1600 mg Serplulimab 300 mg

Q3W, IV, up to 2 years

Primary endpoints:
- **DLT** and **MTD** within 3 weeks after the first administration of HLX26 (i.e. the DLT observation period)

Secondary endpoints:
- Safety
- Pharmacokinetics
- Immunogenicity
- ORR, DCR, DOR, PFS

DCR, disease control rate; DLT, dose-limiting toxicity; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; MTD, maximum tolerated dose; ORR, objective response rate; PFS, progression-free survival; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors.

Results

- As of 19 July 2023, 9 patients were enrolled and received HLX26 at 500 mg (n = 3), 800 mg (n = 3), or 1600 mg (n = 3), in combination with 300 mg serplulimab. All patients had stage IV disease.
- Four (44.4%) patients were diagnosed with non-small cell lung cancer, 2 (22.2%) with small cell lung cancer, 1 (11.1%) with gastric cancer, 1 (11.1%) with cervical cancer, and 1 (11.1%) with endometrial cancer.
- The median age was 66.0 years (range 46–75). Six (66.7%) patients were male.

References

1. Lei Q, *et al.* ***Front Cell Dev Biol*** 2020;21:8:672.
2. Koyama S, *et al.* ***Nat Commun*** 2016;17:7:10501.

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HLX26 plus serplulimab was safe and well tolerated in patients with advanced solid tumours who had failed or could not receive standard therapies. No DLT was reported and the MTD was not determined yet.

Safety

Table 3. Summary of TRAEs[a]

n (%)	500 mg (n = 3)	800 mg (n = 3)	1600 mg (n = 3)
Any TEAE	3 (100)	3 (100)	3 (100)
Grade ≥3 TEAE	1 (33.3)	1 (33.3)	0
Serious TEAE	2 (66.7)	1 (33.3)	0
TEAE leading to treatment discontinuation	0	1 (33.3)	0
TEAE leading to death	1 (33.3)	0	0
AESI	1 (33.3)	1 (33.3)	3 (100)
Any TRAE[a]	3 (100)	3 (100)	3 (100)
Grade ≥3 TRAE[a]	1 (33.3)	1 (33.3)	0
Serious TRAE[a]	2 (66.7)	1 (33.3)	0
TRAE[a] leading to death	1 (33.3)	0	0
AESI			
Related to HLX26	1 (33.3)	1 (33.3)	3 (100)
Related to serplulimab	1 (33.3)	1 (33.3)	2 (66.7)

Table 4. Most common TEAEs

n (%)	500 mg (n = 3)	800 mg (n = 3)	1600 mg (n = 3)
TEAE (≥3 patients)			
Interleukin level increased	0	2 (66.7)	3 (100)
Fibrin D dimer increased	2 (66.7)	1 (33.3)	0
Anaemia	1 (33.3)	2 (66.7)	0
Adrenal insufficiency	1 (33.3)	1 (33.3)	1 (33.3)
ALT increased	1 (33.3)	1 (33.3)	1 (33.3)
Hyperuricaemia	1 (33.3)	1 (33.3)	1 (33.3)
Hyperadrenocorticism	0	1 (33.3)	2 (66.7)
Grade ≥3 TEAE			
Asthenia	0	1 (33.3)	0
Death	1 (33.3)	0	0
Neutrophil count decreased	0	1 (33.3)	0
Pain	0	1 (33.3)	0

[a] Related to both HLX26 and serplulimab.
Groups 500 mg/800 mg/1600 mg refer to HLX26 500 mg/800 mg/1600 mg + serplulimab 300 mg, respectively.
AESI, adverse event of special interest; ALT, alanine aminotransferase; DLT, dose-limiting toxicity; MTD, maximum tolerated dose; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

- All patients experienced treatment-emergent adverse events (TEAEs; Table 3). The most common TEAEs were shown in Table 4.
- The most common adverse events of special interest were interleukin level increased (0% vs 33.3% vs 100%) and hyperadrenocorticism (0% vs 33.3% vs 66.7%).
- All TEAEs that occurred during the DLT observation period were grade 1 or 2.
- No DLT was reported and the MTD was not determined yet.

- Baseline demographics and characteristics are shown in Table 1.

Table 1. Patient demographics and baseline characteristics

	500 mg (n = 3)	800 mg (n = 3)	1600 mg (n = 3)
Median age (range), yr	66.0 (46–73)	68.0 (50–75)	60.0 (57–70)
Sex, n (%)			
Male	2 (66.7)	2 (66.7)	2 (66.7)
Female	1 (33.3)	1 (33.3)	1 (33.3)
ECOG PS, n (%)			
0	1 (33.3)	0	0
1	2 (66.7)	3 (100)	3 (100)
Stage IV, n (%)	3 (100)	3 (100)	3 (100)
Primary tumour, n (%)			
NSCLC	0	2 (66.7)	2 (66.7)
SCLC	1 (33.3)	0	1 (33.3)
Gastric	1 (33.3)	0	0
Cervical	1 (33.3)	0	0
Endometrial	0	1 (33.3)	0
Prior antitumour therapies, n (%)			
Surgery	2 (66.7)	1 (33.3)	1 (33.3)
Radiotherapy	2 (66.7)	2 (66.7)	1 (33.3)
Systemic therapy			
Chemotherapy	3 (100)	3 (100)	3 (100)
Immunotherapy	1 (33.3)	3 (100)	2 (66.7)
Targeted therapy	2 (66.7)	3 (100)	1 (33.3)
Others	1 (33.3)	1 (33.3)	0
Prior lines of therapy, n (%)			
Adjuvant	1 (33.3)	0	1 (33.3)
1	3 (100)	3 (100)	3 (100)
2	2 (66.7)	3 (100)	2 (66.7)
3	1 (33.3)	1 (33.3)	0
4	1 (33.3)	1 (33.3)	0

Groups 500 mg/800 mg/1600 mg refer to HLX26 500 mg/800 mg/1600 mg + serplulimab 300 mg, respectively.
ECOG PS, Eastern Cooperative Oncology Group performance status; NSCLC, non-small cell lung cancer; SCLC, small cell lung cancer; yr, year.

Preliminary Efficacy

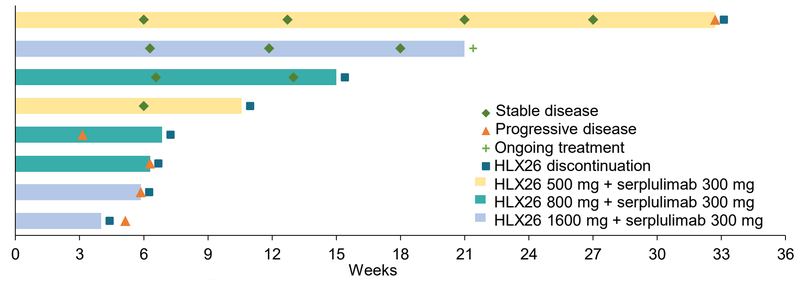
Table 2. Best tumor response in response-evaluable set[a]

	500 mg (n = 2)	800 mg (n = 3)	1600 mg (n = 3)
DCR, % (95% CI)	**50.0** (1.3–98.7)	**33.3** (0.8–90.6)	**33.3** (0.8–90.6)
CR[b], n (%)	0	0	0
PR[b], n (%)	0	0	0
SD[c], n (%)	1 (50.0)	1 (33.3)	1 (33.3)
PD, n (%)	0	2 (66.7)	2 (66.7)
NE, n (%)	1 (50.0)	0	0

- Among these 8 patients, median follow-up duration was 4.8 months.
- Three (37.5%) patients (one in each group) had a best overall response of stable disease.
- None had achieved objective response.

[a] 1 patient (HLX26 500 mg + serplulimab 300 mg) did not have post-baseline tumour assessment, and was excluded from the response-evaluable set; [b] unconfirmed; [c] last for ≥12 weeks. CI, confidence interval; CR, complete response; DCR, disease control rate; NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease.

Figure 2. Swimmer plot showing time on treatment, and time to best response assessed by investigators



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