Poster #294: Safety, pharmacokinetics, pharmacodynamics and preliminary efficacy of HLX301, a bispecific antibody targeting PD-L1 and TIGIT, in patients with advanced solid tumors

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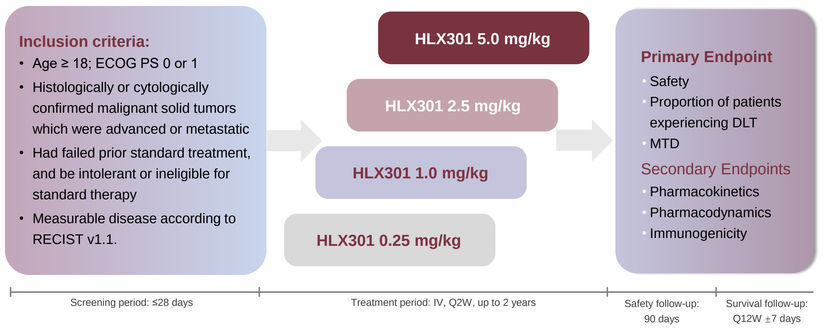
Background

- Bispecific antibodies (bsAbs) provide a novel approach to antitumor therapy by allowing the simultaneous targeting of different antigens via a range of mechanisms of action[1,2]. Currently, multiple bsAbs have been approved for the treatment of hematological malignancies and selected solid cancers with notable clinical efficacy[3].
- Immune checkpoint proteins, the programmed death ligand 1 and T cell immunoreceptor with immunoglobulin and ITIM domain, are important components of cancer-related T cell immunosuppression[4,5].
- HLX301 is a recombinant humanized anti-PD-L1 and anti-TIGIT bispecific antibody. Preclinical studies demonstrated its anti-tumor activity.
- Here we report findings from the dose escalation part (phase 1a) of a phase 1/2 study evaluating HLX301 in patients with locally advanced or metastatic solid tumors.

Methods

- This is a multicenter, first-in-human, open-label, phase 1/2 study to evaluate the safety and preliminary anti-tumor efficacy of HLX301 as a single-agent in patients with locally advanced or metastatic solid malignancies, who had failed or were intolerant to standard therapy, or for whom no standard therapy was available (NCT05102214).
- The study comprised three parts: a phase 1a dose escalation stage (presented in Figure 1), a phase 1b dose expansion stage and a phase 2 clinical expansion stage.
- Tumor imaging by computed tomography or magnetic resonance imaging was scheduled at baseline, every 6 weeks for 24 weeks from the first dose, every 8 weeks thereafter. Tumor response status was assessed using the RECIST v1.1 and immune-based RECIST criteria (response evaluation of hepatocellular carcinoma was per the modified RECIST criteria).

Figure 1. Study design for phase 1a



DLT, dose-limiting toxicity; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; MTD, maximum tolerable dose; Q2W: every 2 weeks; Q12W: every 12 weeks; RECIST, Response Evaluation Criteria in Solid Tumors.

Results

- As of the data cut-off date of Oct 27, 2023, 9 patients were enrolled in the HLX301 0.25 mg/kg (n = 3), HLX301 1.0 mg/kg (n = 3), HLX301 2.5 mg/kg (n = 1), HLX301 5.0 mg/kg (n = 2) cohorts.
- The median duration of HLX301 treatment was 10.3 (range, 0.1–45.1) weeks.
- Baseline demographics and characteristics of the various cohorts are shown in Table 1.

References

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HLX301 showed an acceptable safety profile with preliminary anti-tumor activity. These findings could support further clinical investigation.

Safety

Table 3. Summary of TEAEs

n (%)	0.25 mg/kg (n = 3)	1.0 mg/kg (n = 3)	2.5 mg/kg (n = 1)	5.0 mg/kg (n = 2)
Any TEAEs	3 (100)	3 (100)	1 (100)	2 (100)
Grade ≥ 3 TEAEs	1 (33.3)	1 (33.3)	1 (100)	1 (50.0)
Serious TEAEs	0	1 (33.3)	1 (100)	1 (50.0)
TEAEs leading to Tx discontinuation	0	0	0	1 (50.0)
TEAEs leading to death	1 (33.3)	1 (33.3)	1 (100)	0
Any TRAEs	1 (33.3)	2 (66.7)	1 (100)	2 (100)
Grade ≥ 3 TEAEs	0	0	0	1 (50.0)
Serious TRAEs	0	0	0	1 (50.0)
TRAEs leading to Tx discontinuation	0	0	0	1 (50.0)
TRAEs leading to death	0	0	0	0
IRRs	0	1 (33.3)	1 (100)	0
irAEs	1 (33.3)	1 (33.3)	0	2 (100)

irAE, immune-related adverse event; IRR, infusion-related reactions; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event; Tx, treatment.

Table 4. Most common TEAEs

n (%)	0.25 mg/kg (n = 3)	1.0 mg/kg (n = 3)	2.5 mg/kg (n = 1)	5.0 mg/kg (n = 2)
Any TEAEs (≥ 2 patients[a])				
Cough	0	3 (100)	1 (100)	0
Disease progression	1 (33.3)	1 (33.3)	1 (100)	0
Non-cardiac chest pain	1 (33.3)	2 (66.7)	0	0
Chills	1 (33.3)	1 (33.3)	0	0
Fatigue	1 (33.3)	1 (33.3)	0	0
Abdominal pain	2 (66.7)	0	0	0
Constipation	1 (33.3)	1 (33.3)	0	0
Nausea	0	0	1 (100)	1 (50.0)
Vomiting	2 (66.7)	0	0	0
Arthralgia	1 (33.3)	0	0	1 (50.0)
IRR	0	1 (33.3)	1 (100)	0

[a] *Out of the total 9 patients.*
IRR, infusion-related reactions; TEAE, treatment-emergent adverse event.

- All patients experienced at least one TEAE (Table 3). TEAEs leading to death occurred in 3 (33.3%) patients; all of which were due to disease progression and not related to HLX301.
- 1 patient (11.1%) in the 5.0 mg/kg cohort reported dose-limiting toxicity with a grade 3 cytokine release syndrome that was treatment-related; this was the only patient with the TRAE that led to treatment discontinuation (Table 3). The maximum tolerable dose in this phase 1a was not determined.
- 4 (44.4%) patients reported treatment-related irAEs while treatment-related IRRs occurred in 2 (22.2%) patients (Table 3).
- The most common TEAEs (occurred in ≥ 2 patients) are listed in Table 4.

Table 1. Patient demographics and baseline characteristics

	0.25 mg/kg (n = 3)	1.0 mg/kg (n = 3)	2.5 mg/kg (n = 1)	5.0 mg/kg (n = 2)
Median age (range), years	75 (42–77)	64 (46–72)	72 (72–72)	60.5 (47–74)
Sex				
Male	1 (33.3)	1 (33.3)	1 (100)	1 (50.0)
Female	2 (66.7)	2 (66.7)	0	1 (50.0)
Race				
White	3 (100)	3 (100)	1 (100)	2 (100)
ECOG PS				
0	0	3 (100)	0	1 (50.0)
1	3 (100)	0	1 (100)	1 (50.0)
Tumor staging				
Stage IIIB	0	1 (33.3)	0	0
Stage IV	1 (33.3)	1 (33.3)	1 (100)	2 (100)
Stage IVB	2 (66.7)	1 (33.3)	0	0
Metastatic disease				
Yes	3 (100)	2 (66.7)	1 (100)	2 (100)
No	0	1 (33.3)	0	0
Prior surgery/procedure	1 (33.3)	2 (66.7)	1 (100)	2 (100)
Prior systemic therapy	3 (100)	3 (100)	1 (100)	2 (100)
Anti PD-(L)1	1 (33.3)	1 (33.3)	1 (100)	0
Prior lines of therapy				
Adjuvant/Neoadjuvant	0	1 (33.3)	1 (100)	0
1st-line	3 (100)	2 (66.7)	0	2 (100)
2nd-line	3 (100)	1 (33.3)	0	1 (50.0)
3rd-line	3 (100)	1 (33.3)	1 (100)	2 (100)
4th-line	1 (33.3)	1 (33.3)	1 (100)	2 (100)
5th-line	1 (33.3)	0	0	1 (50.0)
6th-line	1 (33.3)	0	0	0

All data are shown as n (%), unless otherwise stated.
ECOG PS, Eastern Cooperative Oncology Group performance status; PD-(L)1, programmed death-(ligand) 1.

Preliminary efficacy

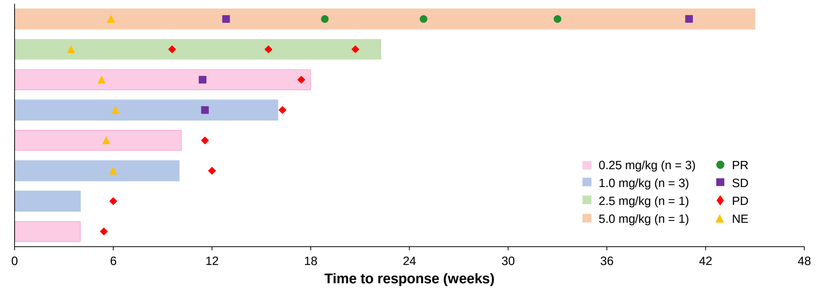
Table 2. Tumor response in the response-evaluable patients[a]

n (%)	0.25 mg/kg (n = 3)	1.0 mg/kg (n = 3)	2.5 mg/kg (n = 1)	5.0 mg/kg (n = 1)
ORR, %	0	0	0	1 (100)
DCR, %	1 (33.3)	1 (33.3)	0	1 (100)
CR	0	0	0	0
PR	0	0	0	1 (100)
SD	1 (33.3)	1 (33.3)	0	0
PD	2 (66.7)	2 (66.7)	1 (100)	0
NE	0	0	0	0

- Among the 8 efficacy-evaluable patients, there were no complete responses.
- One patient in the HLX301 5.0 mg/kg cohort achieved partial response with a DOR of 5.1 months.
- One patient each in the 0.25 mg/kg and 1.0 mg/kg cohort achieved stable disease.

[a] *Confirmed tumor response assessed per RECIST v1.1 for the 8 response-evaluable patients.*
CI, confidence interval; CR, complete response; DCR, disease control rate; DOR, duration of response; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.

Figure 2. Swimmer plot of patients' confirmed tumor response as assessed by the IRRC per RECIST v1.1



NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease.

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