Safety, pharmacokinetics (PK), pharmacodynamics (PD), and preliminary efficacy of HLX301, a bispecific antibody targeting PD-L1 and TIGIT, in patients with advanced solid tumors

Investigators names

Background

Immune checkpoint proteins PD-L1 and TIGIT are important components of cancer-related T cell immunosuppression. HLX301 is a humanized, bispecific IgG1 antibody targeting PD-L1 and TIGIT that showed anti-tumor activity in preclinical studies. A phase 1/2 first-in-human study was conducted to evaluate HLX301 monotherapy in patients with advanced solid tumors (NCT05102214). Here we report findings from the dose escalation part (phase 1a).

Method

This multicenter study enrolled patients with locally advanced or metastatic solid tumors who had failed or were intolerant to standard therapy, or for whom no standard therapy was available. Phase 1a evaluated doses of 0.25-15 mg/kg IV Q2W. Primary endpoints included safety, dose-limiting toxicity (DLT), and maximum tolerated dose (MTD). Secondary endpoints included PK, PD, and immunogenicity.

Results

As of Oct 27, 2023, 9 patients were enrolled (0.25 mg/kg, 3; 1 mg/kg, 3; 2.5 mg/kg, 1; 5 mg/kg, 2). Patients were all White, 55.6% female, median age 72.0 yrs; 88.9% had metastatic disease; all had ECOG PS of 0 (44.4%) or 1 (55.6%). All patients had prior systemic cancer treatment, including 3 (33.3%) treated with PD-(L)1 blockade; 5 (55.6%) patients had ≥ 4 prior lines of therapy. All patients were included in DLT, safety, and PK analyses. Median duration of HLX301 treatment was 10.3 weeks. One patient (11.1%) in the 5 mg/kg cohort reported DLT (grade 3 cytokine release syndrome [CRS]). MTD was not determined. All patients experienced at least one treatment-emergent adverse event (TEAE). TEAEs leading to death occurred in 3 (33.3%) patients, none of these adverse events (AEs) were related to HLX301. Six (66.7%) patients experienced at least one treatment-related adverse event (TRAE). TRAE of grade ≥ 3 was reported in 1 patient (11.1%; grade 3 CRS), who was also the only patient for whom TRAE led to treatment discontinuation. Treatment-related immune-related AEs occurred in 4 (44.4%) patients and treatment-related infusion-related reactions (IRRs) in 2 (22.2%). TRAEs occurring in ≥ 2 patients included IRR (22.2%) and arthralgia (22.2%). HLX301 exhibited linear PK over 0.25-5 mg/kg after single infusion and very limited accumulation after multiple infusions. Mean PD-L1 and TIGIT receptor occupancy in peripheral $CD3^+CD8^+$ cells reached saturation at 5 mg/kg. Anti-drug antibody was detected in 7 patients (77.8%). Among 8 efficacy-evaluable patients, 1 (5 mg/kg cohort) achieved partial response and 2 achieved stable disease; objective response rate and disease control rate per RECIST 1.1 were 12.5% and 37.5%, respectively.

Conclusion

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

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