Preclinical evaluation of HBM7022, an HBICE™ 2+1 CLDN18.2 x CD3 bispecific antibody, for gastric cancer

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Introduction

• Claudin-18.2 (CLDN18.2) is a tetraspan membrane protein involved in the formation of tight junctions. CLDN18.2 is highly expressed in several cancers, including gastric, esophageal, pancreatic, lung, and ovarian cancers.
• CLDN18.2-targeted therapies have shown promising antitumor effects in clinical studies.
• Bispecific T cell engager has the potential to improve the therapeutic window and overcome resistance to targeted therapy. Here we report the development of HBM7022, a CLDN18.2 x CD3 bispecific antibody with our HCAb Based Immune Cell Engager (HBICE™) 2+1 platform. HBM7022 induces potent and specific killing of gastric cancer cells in both in vitro and in vivo studies.

Results

HBM7022: A 2+1 CLDN18.2 x CD3 Bispecific Antibody

HBICE™ heterodimeric bispecific antibodies can be easily manufactured and purified by standard methods such as protein A and ion exchange chromatography

Anti-CD3:
• Optimized anti-CD3 for less cytokine release
• Monkey cross-reactivity

Fc:
• Eliminated FcyR reactivity
• Half-life extension
Tandem anti-CLDN18.2 VH:
• High avidity binding
• Fully human heavy chain only antibody

HBM7022 selectively kills tumor cell lines with high CLDN18.2 expression in vitro

Activity of HBM7022 was assessed with T cell-dependent cellular cytotoxicity (TDCC) assays. Cell lines were mixed with human pan-T cells at E:T of 5:1, then treated with antibodies for 48 hrs. ND, Not determined.

HBM7022 decreases established gastric tumor size

Antitumor activity of HBM7022 against established NUGC4 xenograft tumors; NUGC4 gastric cancer cells and human PBMC were co-injected subcutaneously into NCG mice and allowed to grow to 100-150 mm³. Treatment was administered by intravenous bolus injection on days 4.

Conclusions

HBM7022 is a HBICE™ 2+1 CLDN18.2 x CD3 bispecific antibody:
• The bispecific antibody is easily manufactured and purified.
• It triggers little to none cytokine release in in vitro cytokine release assays.
• It Induces potent and specific killing of gastric cancer cells in both in vitro and in vivo studies.
These results support clinical testing of HBM7022 as a potential therapeutic option for patients with CLDN18.2+ gastric cancer.