A novel class of Innate Cell Engagers targeting NKp30

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Introduction

Cancer immunotherapies have demonstrated remarkable clinical benefits and durable responses even for late-stage cancers. Most of the attempts of current therapies in development are focused on harnessing the adaptive immune system by unleashing antitumor T cell responses. However, there is emerging evidence that cancers develop multiple strategies to escape T cell recognition, hence approaches that do not require T cell recognition should be explored. Tumors can be effectively eradicated by natural killer (NK) cells that can elicit potent anti-tumor response in both mouse cancer models and patients. Therefore exploiting therapies that enhance NK response for the treatment of cancer represents a promising and complementary approach to current existing immunotherapies.

Mechanism of action of Compass multi-specific antibodies

➢ Target one or more tumor-associated antigens (TAA)
➢ Engage CD16A through Fc to drive ADCC
➢ Trigger NK cell activation through NKp30 to synergistically amplify CD16A response or maintain activity in the absence of CD16A expression on NK cells

Compass NKp30 Fab Binds at similar epitope and orientation as ligand B7-H6

Solved co-crystal structure of CTX-NKp30 Fab bound to human NKp30

Compass NKp30xBCMA Lead CTX-8573 induces highly potent and selective lysis of BCMApos tumor cells expressing different levels of antigen

Pharmacokinetics and safety toxicity profile of NKp30xBCMA in cynomolgus monkeys

Serum concentrations of NKp30xBCMA after single i.v. dose

No systemic induction of C reactive protein

NKp30xCD38 with enhanced potency compared to Daratumumab

Differential NK cell activation induced by NKp30xBCMA as compared to BCMA-IgG1 monoclonal

Activity of NKp30 engagers in the absence of CD16A engagement

Compass NKp30xHer2 lead has enhanced activity compared to trastuzumab against tumor cells with wide range of Her2 expression

Compass NKp30xPSMA enhanced NK cells activity towards PSMApos prostate cancer cells

Summary

➢ Compass has developed a novel class of Innate Cell Engagers that bind to antigens on the surface of tumor cells and engage both NKp30 and CD16A on NK cells.

➢ Compass NKp30 engagers can induce killing of tumor cells expressing different levels of tumor antigen without off-target effects and NK cell depletion.

➢ Compass Innate Cell Engagers display PK similar to monoclonal antibodies and favorable toxicity profile.

➢ Our results provide the rationale for developing multifunctional NK p30 engagers for the treatment of hematological and solid tumors.