Preclinical specificity and activity of CABA-201, a fully human 4-1BB containing CD19 CAR T therapy for treatment-resistant autoimmune disease

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Abstract

Over 4% of the world population is estimated to live with autoimmune disease. Treatment typically requires systemic immunosuppressive therapy that have associated toxicities and are not curative. There is increasing evidence that B cells play a central role in disease pathogenesis, based upon responsiveness of B cells to cell depletion by antibody-based therapeutics; however, responses are typically transient due to the incomplete depletion of B cells in secondary lymphoid tissue. Chimeric antigen receptor (CAR) T cells are a novel gene-engineered cell immunotherapy where a synthetic T cell receptor is expressed to redirect the T cell to a desired target. Several CAR T cell products have been approved by the FDA to modestly reduce disease symptoms. While limited, substantial human studies have established the ability of these products to modestly reduce disease symptoms. An early proof of concept pilot study evaluating IC78 in a tandem CAR formation. CABA-201 generated from primary T cells and activity of CABA-201, and provide a clinically relevant benchmark for dose related potency in clinical studies planned for initiation later this year.

Results

A.

Figure 1. Cytotoxicity of CABA-201 toward CD19 positive target cells.

B. A)

Figure 2. CABA-201 CAR T cells control Nalm6 tumor growth in NSG mice.

C. A)

Figure 4. CABA-201 can be generated from autoimmune patient derived T cells.

D. A)

Figure 5. Autologous patient derived CABA-201 CAR T cells effectively kill their autologous patient target B cells.

Conclusions

- CABA-201 has been specifically engineered for patients with autoimmune diseases
- Fully human CD19 binder in CABA-201 was clinically evaluated in ~20 oncology patients with safety profile appropriate for study in autoimmunity
- CABA-201 demonstrated comparable cytotoxic activity to FMC63 CAR T cells against CD19+ target cells in vitro, and comparable in vivo potency was observed in a dose ranging study in the NGS-NHL tumor model. No evidence of off-target cytotoxic activity of CABA-201 was detected against a panel of selected normal human tissues, and no off-target binding against IC78 was detected in a membrane proteome array, in clinical studies evaluating IC78 in a tandem CAR formation. CABA-201 generated from primary T cells and activity of CABA-201, and provide a clinically relevant benchmark for dose related potency in clinical studies planned for initiation later this year.

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