Deep serological profiling of autoimmune patients treated with anti-CD19 4-1BBz CAR T-cells

D Thompson1 S Wong1 D Pateli1 J R Volkov2 G Schett2 S Basu1 D Nunez1
1: Cabaletta Bio, Philadelphia, PA, USA; 2: Friedrich Alexander University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Erlangen, Germany.

Background
Anti-CD19 chimeric antigen receptor (CAR) T-cell therapy is a ground-breaking emerging treatment modality for severe refractory systemic lupus erythematosus (SLE) and has shown early promise in other diseases, including myositis and systemic sclerosis (SSc). Initial clinical data demonstrate that adoptive transfer of anti-CD19 CAR T-cells induces a sustained reduction or elimination of disease in SLE, myositis, and SSc patients. However, the mechanisms underlying remission are unclear. Our aim was to elucidate serological factors that are associated with resolution of disease in SLE, myositis, and SSc patients following treatment with anti-CD19 4-1BBz CAR T-cells.

Methods
Sera were collected from 8 SLE, 2 myositis, and 3 SSc patients prior to and following anti-CD19 4-1BBz CAR T-cell therapy (N=13). Levels of select antibodies were plotted against time in days elapsed from CAR T-cell infusion. Grey dots represent antibody levels in sera collected from healthy donors. (B) Heatmap displays the log2 ratios of antibody concentration changes from pre-infusion to post-infusion analyzed. Hierarchical clustering of these log-transformed ratios was performed using the unweighted pair group method with arithmetic mean (UPGMA) algorithm and Euclidean distance as the distance metric. Color code for each column represents indication or the time elapsed between pre-infusion and the post-infusion samples.

Conclusions
We report on 8 SLE, 2 myositis, and 3 SSc patients following anti-CD19 4-1BBz CAR T-cell therapy showing sustained reduction or elimination of disease off-therapy (Müller et al., NEJM 2024).

• Serum cytokine data suggest that systemic inflammation is consistently decreased at 3 to 6 months post infusion.
• An expanded panel of SLE-associated antibodies shows a profound drop in some SLE-associated antibodies observed in most patients. A separate panel of Myositis-associated antibodies shows a profound drop in some Myositis-associated antibodies observed in most patients.
• An expanded panel of infectious disease-associated antibodies shows a minimal, if any, impact of anti-CD19 4-1BBz CAR T-cell therapy on pre-existing pathogen humoral immunity.
• The more frequent sampling of serum planned for NCT06121297 will allow for a deeper understanding of anti-CD19 4-1BBz CAR T-cell therapy in various autoimmune diseases.