BETA CELL GUARDIANS: MECHANISM OF ACTION OF SAB-142, AN EMERGING IMMUNOTHERAPY FOR NEW ONSET T1D

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Introduction

Clinical Need — There is no licensed therapy to halt or reverse new-onset Type 1 Diabetes.

- Rabbit anti-thymocyte globulin (rATG) slows the progression of T1D (preserves C-peptide and improves glycemic control).
- rATG it is limited by serum sickness and the formation of neutralizing antibodies.

Multi-specific antibody Solution — SAB-142 is a Fully Human, Multi-Specific, Targeted Anti-Thymocyte Globulin (hATG) for Delaying Onset and Progression of T1D.

- SAB-142 is generated from a unique multi-specific antibody platform.
- SAB-142 binds to multiple T cell surface proteins, similar to rATG.
- No anti-drug antibodies with potential for redosing.
- No Serum Sickness.

Aim of Study — The aim of this study was to characterize SAB-142's pharmacodynamic mechanism of action through immunoprofiling in a first-in-human clinical study.

Study Design

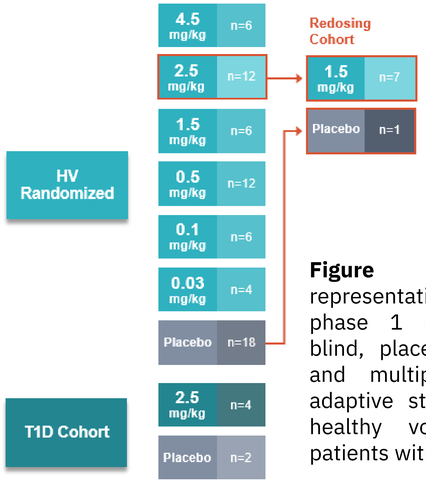
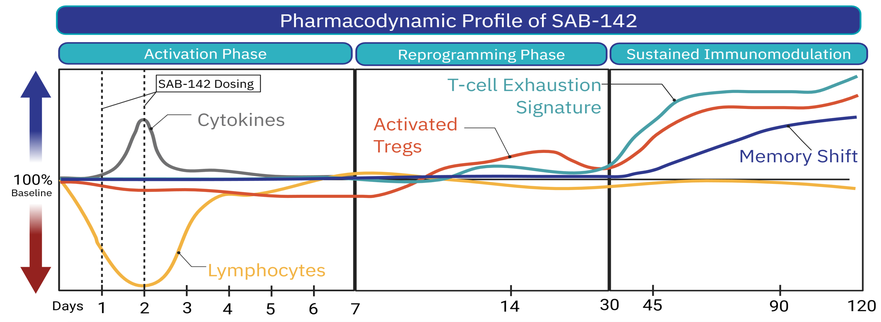
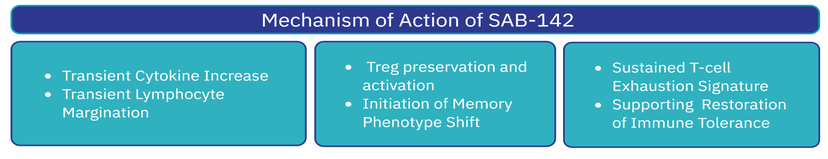


Figure 1. Schematic representation of SAB-142-101 phase 1 randomized, double-blind, placebo-controlled, single and multiple ascending dose adaptive study design including healthy volunteers (HV) and patients with T1D.

Conclusion





Results

SAB-142 Binds to the Same Receptors as rATG

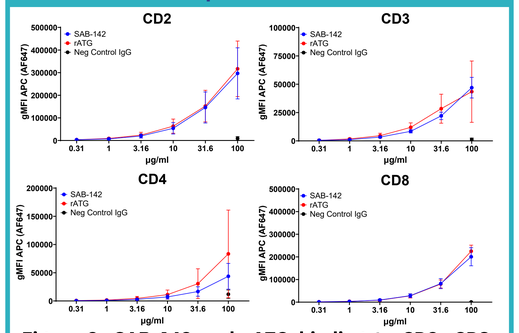


Figure 2. SAB-142 and rATG binding to CD2, CD3, CD4, CD8. Directly labeled SAB-142, rATG or negative control IgG was incubated with Bw cells expressing the indicated T cell surface protein. The cells were analyzed by flow cytometry and data shown is the geometric mean fluorescent intensity with the background from the parental Bw cells subtracted. Error bars show SEM, N=6.

SAB-142 Demonstrates Sustained CD4⁺ T Conv Cell Exhaustion analogous to rATG

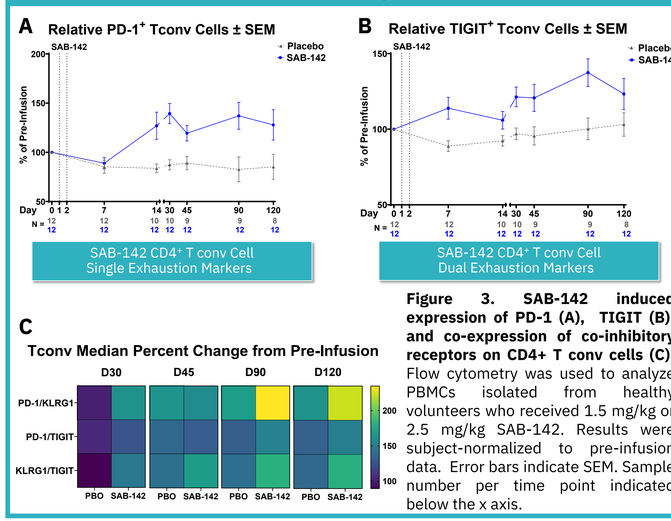


Figure 3. SAB-142 induced expression of PD-1 (A), TIGIT (B), and co-expression of co-inhibitory receptors on CD4+ T conv cells (C). Flow cytometry was used to analyze PBMCs isolated from healthy volunteers who received 1.5 mg/kg or 2.5 mg/kg SAB-142. Results were subject-normalized to pre-infusion data. Error bars indicate SEM. Sample number per time point indicated below the x axis.

SAB-142 Preserves and Activates T Regulatory Cells

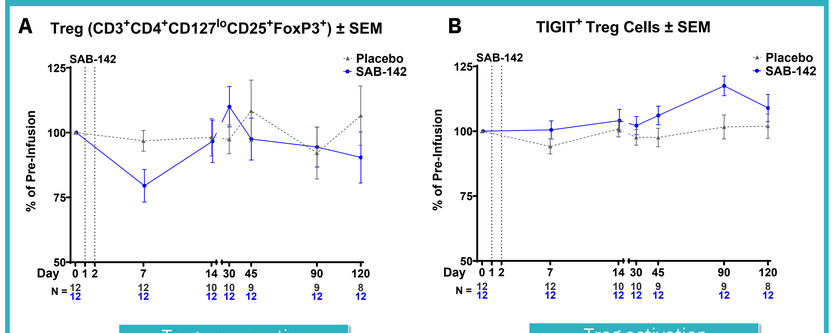


Figure 4. SAB-142 preserves Treg Cells (A) and induces the inhibitory receptor, TIGIT, on Tregs (B). PBMCs were isolated from healthy volunteers who received 1.5 mg/kg or 2.5 mg/kg SAB-142 and subjected to immunophenotyping analysis by flow cytometry. Results shown were subject-normalized to pre-infusion data. Error bars indicate SEM. Sample number per time point indicated below the x axis.

SAB-142 Induces Differentiation from Naïve to a Memory Phenotype

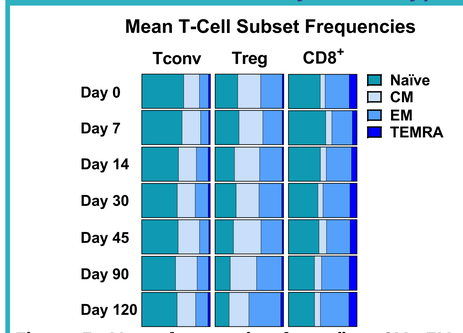


Figure 5. Mean frequencies for naïve, CM, EM, and TEMRA demonstrate phenotypic shifts following SAB-142 treatment in each cell type. PBMCs were isolated from healthy volunteers who received 1.5 mg/kg or 2.5 mg/kg SAB-142 and subjected to immunophenotyping analysis by flow cytometry. Composite bar graphs indicate the portion of Tconv, Treg and CD8+ cell populations identified as Naïve, CM, EM and TEMRA subpopulations.