Safety Profile of SAB-142: A Fully Human Anti-Thymocyte Globulin

Stan Stoyanov, Angie Parizek, Alexandra Kropotova, Thomas Luke, Eric S Sandhurst, and Diane Maher
SAB Biotherapeutics, Sioux Falls, SD 57104

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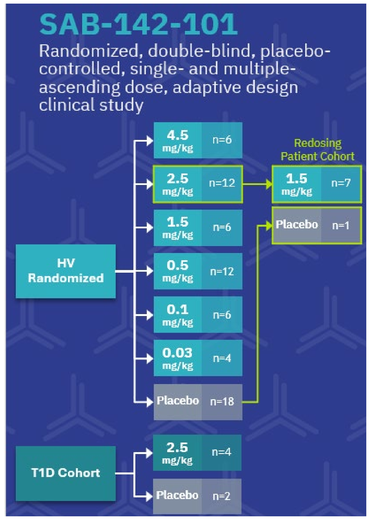
Introduction

- There is no licensed therapy to halt or reverse new-onset Type 1 Diabetes (NOT1D).
- Rabbit anti-thymocyte globulin (rATG) has been evaluated, but is limited by:
  - Neutralizing antibody formation
  - Hypersensitivity reactions
- SAB-142: a fully human, multi-specific anti-thymocyte globulin derived from the SAB Tc Bovine platform.
- Aim: To evaluate safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of SAB-142 in humans and juvenile non-human primates (NHPs).

Methods

Human Study (SAB-142-101)

- Design: Randomized, double-blind, placebo-controlled, Phase I.
- Population: Healthy volunteers + T1D cohort.
- Dosing: Single IV infusion, 0.03–4.5 mg/kg.
- Endpoints: Safety, tolerability, PK, PD.



NHP Study

- Design: GLP study in juvenile cynomolgus monkeys.
- Dosing: Initial and Re-dose with SAB-142, rATG or Placebo.
- Endpoints: Safety, toxicokinetics, immunologic effects.

NHP Study Design

Duration of Observation		9 Months	
		~6 Months	~3 Months
Group	Test Material	Initial Dose (mg/kg)	Re-dose at ~6 months (mg/kg)
1	Placebo Control	0	0
2	Thymoglobulin®	25 (Split over 2 days: 10/15)	25 (Split over 2 days: 10/15)
3	SAB-142	5	50 (Split over 3 days: 20/20/10)
4	SAB-142	10	10
5	SAB-142	25 (Split over 2 days: 10/15)	25 (Split over 2 days: 10/15)

Number of Animals: 3 monkeys/sex per treatment arm: 30 monkeys Total
Test article, active comparator or placebo were administered in a volume of 10 mL/kg and infused over 2 hours via intravenous infusion.

Results:

SAB-142-101 First-in-Human (FIH) Clinical Study: Safety Findings

- No deaths, drug-related SAEs, or study withdrawals.
- No serum sickness.
- Most treatment-related TEAEs were mild in intensity. The most frequent TEAEs (reported in ≥ 4 [10%] participants) included transient lymphopenia, headache, Infusion Related Reactions (IRRs: infusion site phlebitis, Cytokine Release Syndrome, vascular access site thrombosis), nausea, and glycosuria.
- The majority of treatment-related TEAEs were reported between Day 1 and Day 7 post-dose. The TEAEs from Day 8 onwards were comparable in the pooled SAB-142 vs the pooled placebo groups (45.0% and 50.0% of participants, respectively).
- No abnormal findings in neutrophils, erythrocytes, platelets or B cells (see figure 1).
- Lymphocytes: transient peripheral lymphopenia only (margination, not lymphodepletion). All lymphocytes recovered back to the baseline by Day 4 (see figure 2).
- No clinically significant abnormalities in coagulation parameters.
- There were no EKG abnormalities.

Juvenile Non-Human Primate (NHP) Toxicology Study: Safety Findings

- No SAB-142 or rATG-related mortality, organ toxicity, or weight changes.
- No effects on neurobehavior, ECG, urinalysis, or food consumption.
- No increases in pro-inflammatory cytokines (TNF-α, IL-8, etc.).
- Hematology and chemistry: no unexpected findings.
- Only incidental microscopic findings were also seen in controls.

SAB-142-101: SAB-142 does not cause sustained cellular depletion

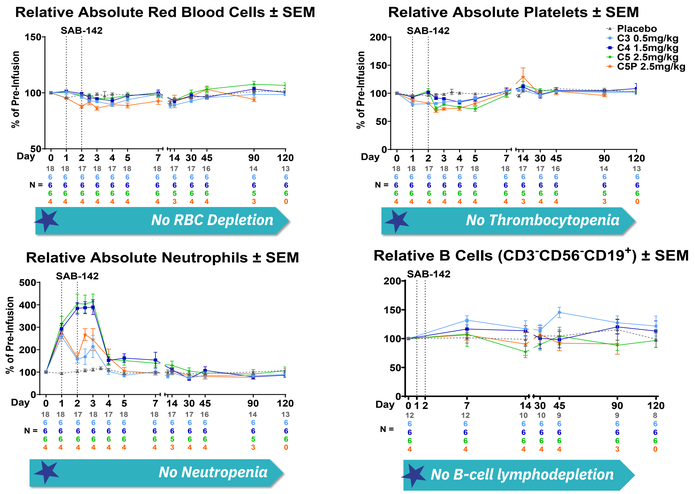


Figure 1. SAB-142 does not cause sustained depletion of red blood cells (RBC), platelets, neutrophils or B cells. Results normalized to pre-infusion sample. C3-C5: Healthy Volunteers; C5P: T1D patients. N indicates number of participants.

SAB-142-101: SAB-142 does not cause sustained lymphodepletion

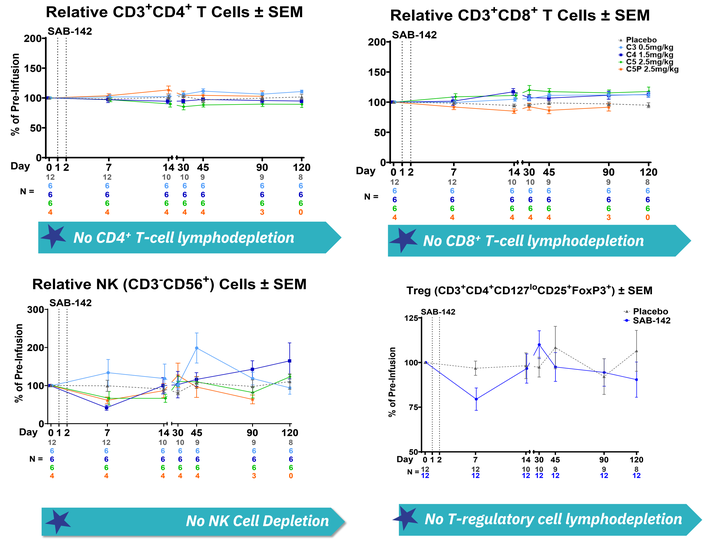


Figure 2. SAB-142 does not cause sustained lymphodepletion. Results normalized to pre-infusion sample. C3-C5: Healthy Volunteers; C5P: T1D patients. N indicates number of participants.

Conclusion

- **FIH**
  - SAB-142 demonstrated a favorable safety profile in humans
  - Well tolerated up to 2.5 mg/kg IV.
  - No drug-related SAEs, withdrawals, serum sickness, or anti-drug antibodies.
- **NHPs**
  - SAB-142 demonstrated a favorable safety profile in Juvenile NHPS
  - Tolerated up to 50 mg/kg with re-dosing after 6 months.
  - NOAEL = 50 mg/kg, corresponding to ~20X human exposure safety margin.
- **Safety & Tolerability**
  - Phase 1 results support the safe use and re-dosing of SAB-142 in the Phase 2B SAFEGUARD study in patients 5-40yo with new-onset T1D.