In Vivo Evaluation of a Bio-Synthetic Whole Blood Analogue (WBA) for Hemorrhagic Shock Resuscitation

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Background

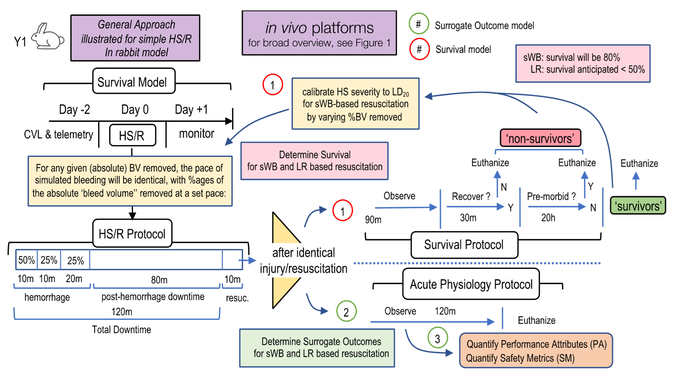
- Hemorrhagic shock remains a principal cause of preventable mortality in battlefield and civilian settings
  - Timely transfusion of fresh whole blood (fWB) or balanced components reduces morbidity and mortality
- Robust efforts are directed at resolving challenges regarding implementation of in-field transfusion
  - Including development of bio-synthetic blood analogues.
- Utilized rabbit survival model of hemorrhagic shock and resuscitation to evaluate performance of a three-component whole blood analogue (WBA) and recent iterations of EM as a standalone component (SAC):

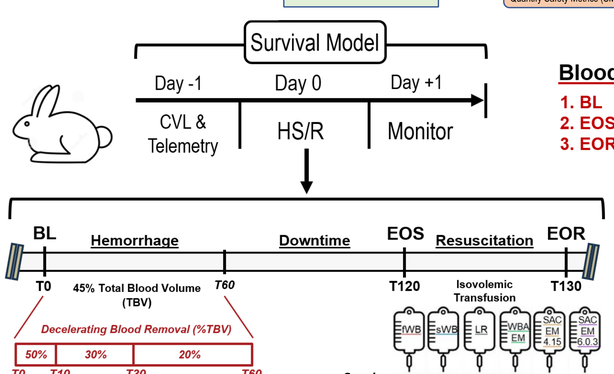
WBA-EM
- RBC Analogue: ErythroMer (EM)
- Platelet Mimetic: SynthoPlate (SP)
- Rabbit Plasma: Freeze-Dried Plasma (FDP)

SAC-EM: $EM_{4.15}$ & $EM_{6.0.3}$
- RBC Analogue: ErythroMer (EM)
- 5% Human Serum Albumin

Goal: Meet progressively restrictive non-inferiority (NI) margins (40% in Y1 to 10% in Y4) compared to stored whole blood (sWB) at 26 days (median in-theater storage duration).

Methods



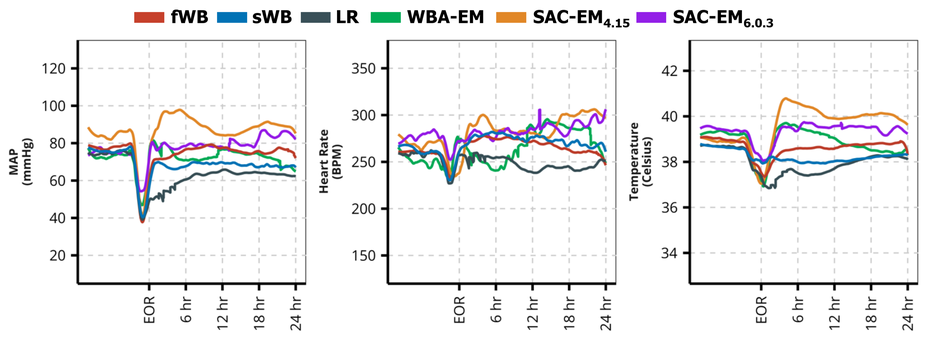


Blood Collection:

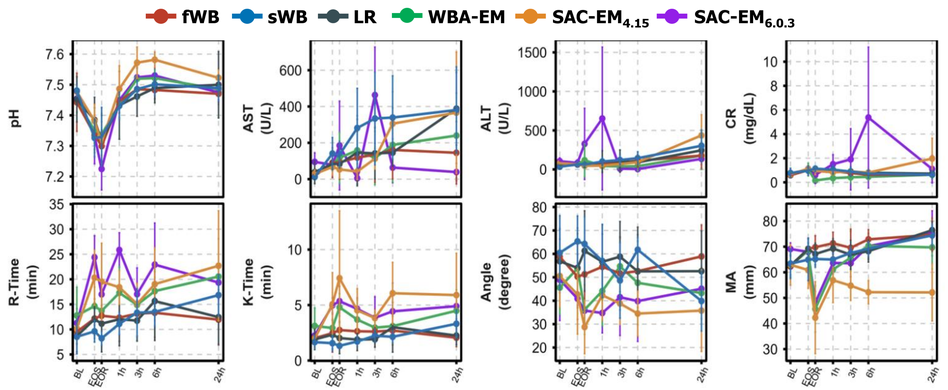
1. BL
2. EOS
3. EOR
4. +1hr
5. +3hr
6. +6hr
7. +24hr

Results

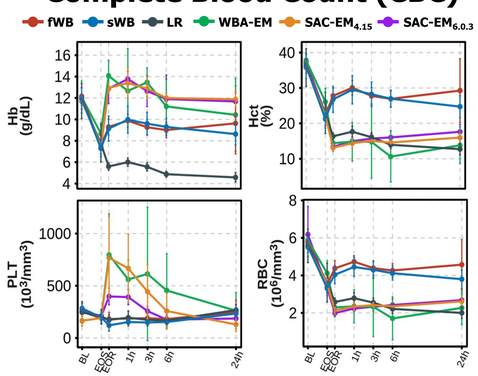
Acute Physiologic Outcomes



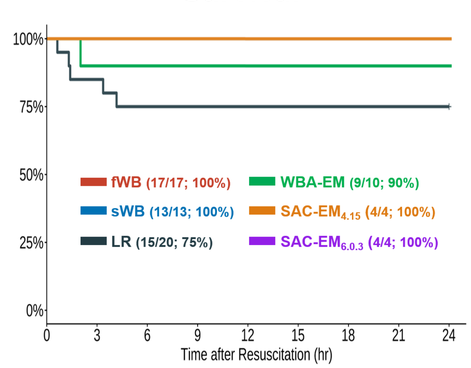
Biochemical, Metabolic, & Coagulation



Complete Blood Count (CBC)



Survival



Non-Inferiority (NI) Analysis

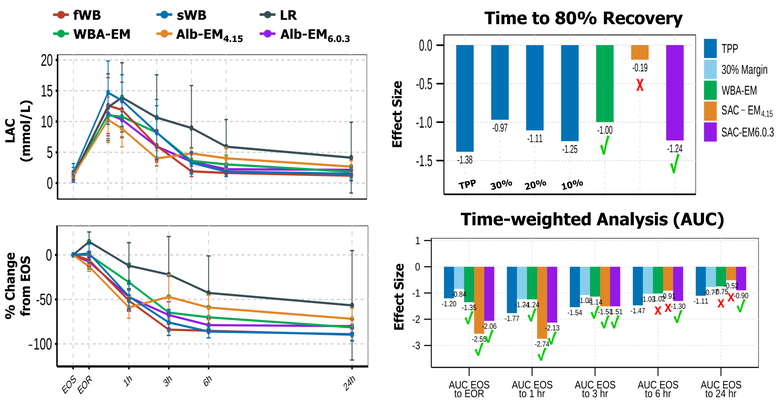
Effect Size: Quantifies **superiority** of:

(A) Stored whole blood (sWB): Target Product Profile (TPP)
(B) Whole blood analogue (WBA)
OVER (C) Lactated Ringer's (LR): negative control

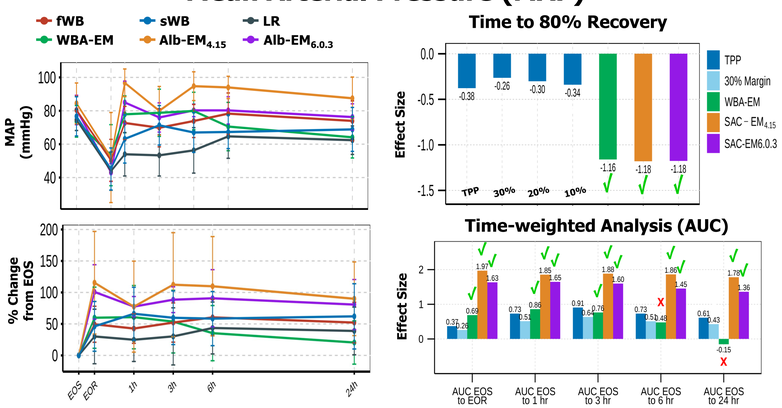
$$\text{Effect Size} = \frac{\text{mean(x)} - \text{mean(LR)}}{\text{SDLR}}$$

TPP Effect Size: determined by comparing performance of sWB and (-) LR groups

Lactate (LAC)



Mean Arterial Pressure (MAP)



Conclusions & Future Directions

- We have demonstrated preliminary intercomponent compatibility and preliminary efficacy of WBA & standalone RBC analogue formulations for resuscitation of severe hemorrhagic shock.
- Ongoing projects will explore dosing ratios and comparative efficacy to stored whole blood in both *in vitro* & *in vivo* models of massive transfusion and complex hemorrhagic shock.

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