

SANGUINATE® Reverses RBC Sickling in Patients with Vaso-Occlusive Crisis of Sickle Cell Disease

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Introduction

Severe Acute Vaso-Occlusive Crisis (VOC) events in sickle cell disease (SCD) patients adversely impacts health and quality of life. Standard of care treatments do not directly *reverse* intra-occlusion caused by red blood cell (RBC) sickling during VOC. SANGUINATE® (PEGylated carboxyhemoglobin, bovine) is a gas transfer agent capable of selective oxygen delivery to hypoxic sites that may unsickle RBCs *in situ*.

Hypothesis

SANGUINATE® will deliver oxygen to sickled RBCs reversing HbS polymerization, thereby promoting recovery of shape to a more normal morphology. SANGUINATE® may promote faster VOC resolution including reduced pain, IV opiates and hospitalization rates in VOC.

Methods

Ex vivo studies: Blood samples from HbS and HbAA volunteers were deoxygenated, mixed with SANGUINATE® or PEGylated albumin control, and then analyzed for reversal of sickling by microscopy and flow cytometry. *Clinical Trial:* Study of SANGUINATE® In the Treatment of SCD Patients with VOC (NCT02411708). Participants were randomized to a SANGUINATE or placebo arm, in addition to standard treatment and IV opioid per institutional practice. Blood samples were collected pre- infusion, at the time of discharge and 72 hours after infusion, and analyzed for reversal of sickling.

Results

SANGUINATE® *ex vivo* treatment of sickled hypoxic SCD RBCs promoted a rapid shift back to a round morphology versus cells treated with PEGylated albumin control. Clinical trial samples from patients receiving SANGUINATE® showed a similar shape-shift that was not observed in placebo arm. Importantly, the shape-shift occurred rapidly and persisted through the 72hr time point.

Conclusion

VOC results from the accumulation of sickled RBC in SCD patients. The unique gas transfer properties of SANGUINATE® resulted in the rapid delivery of oxygen to hypoxic RBCs promoting a shape-shift to round morphology in *ex vivo* controlled experiments and in SANGUINATE® treated VOC patients. Collectively these data support the continued evaluation of SANGUINATE® in VOC patients.