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

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Introduction
Severe Acute Vaso-occlusive (SA-VOC) events in sickle cell disease (SCD) patients adversely impacts health and quality of life. Standard of care treatments do not distinctly reverse intra-ocular RBC sickling during SA-VOC. Newer medications actively promoting RBC unsickling may provide for improved outcomes in SCD. SANGUINATE® (PEGylated carboxyhemoglobin, bovin) is a gas transfer agent capable of selective oxygen (O2) delivery to hypoxic sites that can unsickle RBCs in situ.

Hypothesis
SANGUINATE® will deliver oxygen to sickled RBCs reversing HBO2 polymerization promoting shape change to round morphology. SANGUINATE® can be effectively substituted for IV saline and co-administered with IV opiates. SANGUINATE® may promote faster VOC resolution including reduced pain, IV opiates and hospitalization rates in SA-VOC patients.

Methods
Ex vivo studies: Blood samples were collected from HbS and HbAA volunteers. Samples were deoxygenated and mixed with SANGUINATE® then analyzed for reversal of sickling by microscopy and image-based flow cytometry. Clinical Trial: Study of SANGUINATE® in the Treatment of SCD Patients with VOC (NCT02411708). Blood samples were collected prior to infusion, at time of discharge and 72 hours post discharge to assess the impact of SANGUINATE® upon RBC morphology and inflammatory markers.

Results
SANGUINATE® ex vivo treatment of hypoxic SCD RBCs promoted a rapid shift to a round morphology versus PEGylated albumin control. Clinical trial patient samples from those receiving SANGUINATE® showed a similar shape-shift that was not observed in placebo control subjects. Importantly, shape-shift was observed rapidly with persistence through the 72hr time point.

Conclusion
SA-VOC results from the accumulation of the sickled RBC levels in SCD patients. SANGUINATE® unique gas transfer properties resulted in the rapid delivery of O2 to hypoxic RBCs promoting a shape-shift to round morphology in ex vivo controlled experiments as well as in SANGUINATE® treated patients. Collectively these data support the continued evaluation of SANGUINATE® in SA-VOC patients.

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