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Introduction
Severe acute vaso-occlusive crisis (SA-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 RBC sickling during SA-VOC. Newer medications actively promoting RBC unsickling may provide for improved outcomes in SCD.

Hypothesis
• SANGUINATE® will deliver oxygen to sickled RBCs reversing HbSS 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

Methods
Ex vivo studies: Blood samples were collected from BHS 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 pre-infusion, at the time of patient discharge and 72 hours and analyzed for reversal of sickling.

Results
SANGUINATE® ex vivo treatment of hypoxia 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 accumilation 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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The Conflict of Interest disclosure for above authors have been satisfied.