

Molecular Resolution of an Active Vaso-Occlusive Crisis in VOC Patients Treated with SANGUINATE®.

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SANGUINATE® (PEGylated carboxyhemoglobin bovine) is a gas transfer agent that can deliver oxygen directly to the hypoxic (sickled) RBCs of sickle cell disease (SCD) patients. Importantly, the transfer of oxygen also promotes rapid conversion of the sickled RBCs to a normal morphology. SANGUINATE® is currently being investigated as a clinical candidate for the treatment of acute severe Vaso-Occlusive Crisis (VOC) in SCD patients (NCT02411708).

Consenting SCD patients in acute severe VOC were treated with a single IV infusion of SANGUINATE® (8ml/Kg) with blood samples collected pre-treatment and at two post-treatment points; VOC resolution (discharge time) and 72hrs later. Image-based multi-parameter flow cytometry was performed on all samples (including placebo controls) and the extent of sickled/unsickled cell populations was determined across all enrollees at these time points.

Patient samples treated with SANGUINATE® showed a shift towards a more normal morphology when the pre- and post-VOC resolution samples were compared for each individual. In contrast, the placebo control patient samples showed worsening or no improvement of the sickled/unsickled ratios. Additionally, only patients treated with SANGUINATE® exhibited extended unsickling profiles at 3 days following treatment.

SANGUINATE® was capable of promoting the rapid depolymerization of sickled hemoglobin within peripheral blood samples of severe VOC patients treated with this novel gas transfer agent. Despite a half-life of 18-24hrs SANGUINATE® treated patients continued to exhibit fewer sickled cells at the 72hr sample point. SANGUINATE® can quickly oxygenate patient sickled RBCs effectively reducing both the short-term and long-term sickled RBC levels. Collectively these results support the continued clinical evaluation of SANGUINATE® as a rescue agent for rapid resolution of SCD patients in severe VOC in the ambulatory setting.