PEGylated Carboxyhemoglobin Bovine (SANGUINATE®) Restores RBCs Roundness and Reduces Pain During a Sickle Cell Vaso-Occlusive Crisis

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Background:

Pain during vaso-occlusive crisis (VOC) is a hallmark of sickle cell disease (SCD) as doxycycline (sickled) red blood cells (RBC) aggregate in the microcirculation due to Hemoglobin S (HbS) polymerization. PEGylated carboxyhemoglobin bovine (PEG-COHb; SANGUINATE®) was designed as a gas transfer agent to depolymerize HbS. Prior in vitro studies have shown PEG-COHb capability to transfer oxygen (O2) to SCD doxycycline RBCs, reversing sickling. A prospective, randomized, single-dose Phase II clinical study is in progress (NCT02411708) evaluating the safety and efficacy of PEG-COHb in the treatment of severe VOC including pain reduction in the ambulatory setting. This research reports on the preliminary evaluation of the levels of RBC sickling following treatment and association with pain score.

Methods:

Participants were randomized 2:1 to a PEG-COHb (320 mg/kg) or saline (placebo) arm in equivalent volume. Participants also received study opioids per institutional practice. Pain was assessed using a 10-point pain scale. Blood was collected to assess RBC shape morphology changes using image-based flow cytometry.

Preliminary Clinical Results:

Shift of Global RBC Population After PEG-COHb Infusion

Data Collection: Pain Scores and Blood Samples

Blood was collected at pre-treatment, at TFRD, and at 72-hours post-treatment to test RBC shape, RNA, and Plasma cytokines. RBC shape values and pain scores at pre-infusion and TFRD are presented here.

Key:

- PEG-COHb: PEGylated Carboxyhemoglobin bovine
- Quadrant: TFRD
- Time: Readiness of Discharge

Conclusions:

Global RBC population in 10 of 16 of PEG-COHb-treated participants exhibited increased circularity and decreased symmetry consistent with unsickling observed in ex vivo experiments.

- Low-circularity RBC population from PEG-COHb-treated participants showed greater shape change after infusion compared to saline control (p<0.05).
- Increase to more normal shape values from high- and low-circularity RBC population was correlated only in PEG-COHb participants.
- 8 of 14 of PEG-COHb-treated participants exhibited 40% or greater decrease in pain scores and increased RBC circulation between pre-infusion and time for readiness of discharge compared to 0 of 7 participants in saline cohort (p=0.02).

Results warrant further clinical development of PEG-COHb (SANGUINATE®) for the treatment of acute vaso-occlusive crisis in sickle cell patients.

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The Conflicts of Interest disclosures for all authors have been satisfied.