

USE OF PEGYLATED-CARBOXYHEMOGLOBIN BOVINE FOR THE TREATMENT OF SICKLE CELL DISEASE ASSOCIATED LEG ULCERS: RESULTS FROM A PHASE 2 SAFETY STUDY

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Background

Leg ulcers are a common complication of sickle cell disease (SCD). The pathophysiology of SCD leg ulcer is complex and may include obstruction of blood vessels by sickled red cell, chronic anemia, depleted nitric oxide bioavailability (resulting in impaired endothelial function), infection, thrombosis and excessive vasoconstriction. These events lead to progressive peripheral de-vascularization and tissue necrosis, such that even minor lower-leg wounds can become persistent ulcers, with no tendency to heal after months of appropriate treatment.

PEGylated-Carboxyhemoglobin bovine (PEG-CO₂Hb; SANGUINATE) is an oxygen carrying agent with anti-inflammatory activity. A study of safety and effectiveness was undertaken in SCD patients with chronic leg ulcers to determine the safety of this investigational drug administered in as a once weekly infusion for either 4 or 6 weeks.

Aims

To assess the safety and efficacy of repeated doses of PEG-CO₂Hb on SCD leg ulcers.

Methods

The study was an escalating, repeated-dose, open-label, Phase 2 study to test PEG-CO₂Hb at 320 mg/kg (8 mL) in subjects suffering from leg ulceration associated with SCD. It was conducted in Panama and the Dominican Republic. All enrolled subjects underwent a 3-week Run-In Period, during which they received standard of care treatment for wound management. During the Treatment Period, subjects were assigned sequentially to Cohort 1 or Cohort 2. Cohort 1 received 4 once-weekly doses by 2-hour intravenous infusion of SANGUINATE. Following the completion of Cohort 1, the safety findings were reviewed prior to initiating Cohort 2. Cohort 2 received 6 once-weekly infusions. In addition to the study drug, subjects continued to receive standard of care during the Treatment Period. One week after the end of Treatment, subjects returned to the study center for a Final Visit.

The following assessments were done:

- Safety: Safety was assessed by recorded adverse events (AEs), laboratory assessments (hematology, chemistry, and urinalysis), vital signs, concomitant medications, and 12-lead electrocardiograms (ECGs).
- Efficacy: Wound pain, wound appearance and condition, wound size, wound vascular status (Venous Clinical Severity Score; VSSC)

- Quality of Life: Quality of life was assessed using the Short Form-12 v2 Health Survey (SF-12).

Results

The administration of once-weekly infusions of PEG-COHB was well tolerated. Treatment emergent adverse events (mild pyrexia, moderate worsening anemia) considered related to study drug were report in 2/10 patients. Increases in mean arterial pressure were anticipated due to the oncotic effects of this colloidal drug, but with no consistent pattern to the changes. Changes in ECG intervals were seen in a few subjects, but those changes were not considered clinically meaningful. There were no clinically meaningful changes in laboratory values, physical examinations, or concomitant medications.

There were no statistically significant changes from Baseline in leg ulcer pain and wound surface area for either Cohort. All of the wound assessments remained relatively consistent throughout the study. There were slight decreases in total VCSS at most time points, indicating slight improvement in vascular status. Results were similar for the individual scores.

Conclusion

The administration of 4 or 6 once-weekly infusions of PEG-COHB at a dose of 320 mg/kg was generally well tolerated. Slight improvements in total and individual VCSS are promising and may warrant further study with prolonged repeated doses of PEG-COHB.

Key words: sickle cell disease, leg ulcer, oxygen therapeutic

Category. 25. Sickle Cell disease

Goal of abstract: SCD continues to be a growing problem in EU due to immigration such that EHA has included separate category for SCD. This is the only data available for EHA – hence the recommendation to submit here. Also there is no other appropriate info to submit on SG at this time. PI and P2 of bnao are suggested to be presented in the US and therefore must be sequestered.

Instructions to author: <http://www.ehaweb.org/assets/Congress/EHA22/EHA22-Abstract-Submission-Terms-Conditions-January.pdf>

Number of characters with spaces: 3600

Note: this abstract has been submitted to FSCDR; under general abstract guidelines, abstracts submitted to regional hematology meetings can be submitted to EHA. It has been modified to meet EHA guidelines