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Corresponding Author:	Peter Buontempo Prolong Pharmaceuticals South Plainfield, New Jersey UNITED STATES
Corresponding Author's Institution:	Prolong Pharmaceuticals
Order of Authors:	Peter Buontempo
	Hemant Misra
	Gladys Maria Paulino
	Lineth Lopez
Additional Information:	
Question	**Response**
Enter the first nine (9) digits of the Transaction ID from the email receipt from Integrative Educational Solutions.	204161680
First Author:	Peter Buontempo
Corresponding Author E-Mail:	jvalentino@prolongpharma.com

A Phase 2 Safety Study of SANGUINATE in Patients with Leg Ulcers

Lineth Lopez MD, Gladys Maria Paulino MD, and Hemant Misra PhD.

Introduction

Leg ulcers are a serious and debilitating complication of sickle cell disease (SCD). It is estimated that leg ulcers develop in 10% or more of people with sickle cell disease during their lifetime. Chronic tissue hypoxia, hemolysis and inflammation result in a cascade of events leading to progressive de-vascularization and tissue necrosis resulting in chronic wounds that show no tendency to heal after months of appropriate treatment.

SANGUINATE is an oxygen carrying agent with anti-inflammatory activity. A safety study 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.

Methods

The study was conducted in Panama and the Dominican Republic. This was an escalating, repeated-dose, open-label, Phase 2 study to test SANGUINATE at 320 mg/kg (8 mL) in subjects suffering from leg ulceration associated with SCD. All enrolled subjects underwent a 3-week Run-In Period, during which they received standard of care treatment for the wound management. During the Treatment Phase subjects were assigned sequentially to Cohort 1 or Cohort 2. Cohort 1 received 4 doses, once-weekly, 2-hour intravenous (IV) infusions of SANGUINATE 320 mg/kg. Following the completion of Cohort 1, the safety findings were reviewed prior to initiating Cohort 2. Cohort 2 received once-weekly infusions for 6 weeks. In addition to the study drug, subjects continued to receive standard of care during the Treatment Period. One week after the end of the Treatment Phase, 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; VSCC)
- 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 SANGUINATE was well tolerated. 2/10 patients report treatment emergent adverse events considered related to study drug. Mean

changes for blood pressure did show some increases due to oncotic and colloidal nature of drug, but there was not a consistent pattern to those 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 SANGUINATE 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.