

Abstract Submission

28. Transfusion medicine

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USE OF A PEGYLATED CARBOXYHEMOGLOBIN BOVINE IN SEVERE LIFE-THREATENING ANEMIA

Ronald Jubin*¹, John Berryman¹, Richard Prince¹, Hemant Misra¹, Abraham Abuchowski¹

¹Prolong Pharmaceuticals, Prolong Pharmaceuticals, South Plainfield, United States

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Background: Patients who cannot receive blood transfusions in the presence of severe anemia can sustain significant morbidity and mortality. Religious beliefs and hemolytic reactions are the most common reasons for not transfusing a patient. Pegylated bovine carboxyhemoglobin (Sanguinate; SG), a therapeutic drug, has been used in 5 such patients including a patient who developed a severe hemolytic reaction following stem cell transplantation. SG is a therapeutic drug designed to carry carbon monoxide (CO) and oxygen in the mammalian vasculature for delivery to tissues to synergistically treat inflammation and vasoconstriction and other comorbidities characterized by tissue hypoxia.

Aims: Perform post-hoc analysis of clinical findings; their relationship to individual patient diagnosis/associated comorbidities and SG intervention.

Methods: Five patients with hemoglobin (Hb) levels under 3.5 g/dL were treated with repeated doses of SG. Diagnoses included AML, hemolytic reaction, acute chest syndrome and sickle cell crisis. Patients ranged in age from 19 to 61. A unit of SG consists of 500 mL (40 mg/mL). Total doses ranged from 1 unit/day for 2 to 4 days up to 8 units given over 9 days.

Results: No adverse events associated with SG were reported. Each investigator reported clinical improvements in their patient following administration of SG, despite continuing low Hb levels. The number and size of allowed blood draws were restricted; therefore analysis of clinical chemistries was limited. Patients with reported extreme fatigue or neurological deficit each demonstrated increases in responsiveness or self-reported comfort within close temporal association with SG treatment. One patient had a significant increase in cerebral oximetry and another showed improvements in cerebral blood flow measured by TCD. A patient with hyperhemolysis reported feeling well with no pain and no shortness of breath despite severe anemia (Hb 2.5) and had improved mobility following a total of 8 units of SG. A patient who had undergone a stem cell transplant developed immune hemolytic anemia, with resulting extreme fatigue and tachycardia. He received 4 once-daily units of SG, during which time his heart rate normalized and was reported to be alert and oriented.

Summary/Conclusion: Evidence indicates that SG has potential therapeutic benefit in patients who have life-threatening anemia and cannot receive blood transfusions for personal or medical conditions. As vasoconstriction, inflammation, and oxygen deprivation are significant factors in severe hemolysis and ischemia, SG through the therapeutic actions of CO and oxygen may interrupt the ischemic cascade and improve clinical symptoms of hypoxia due to severely low hemoglobin levels. The improved clinical status in these patients suggests that SG has potential utility in patients with severe anemia who are unable to receive blood transfusions. Since submission to ASCO2015, preclinical and *in vitro* studies with SG have been shown to demonstrate anti-inflammatory activity as well as active CO and oxygen transfer. SG is currently in clinical development. A protocol is under development to treat patients for whom blood transfusion is not an option.

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