The USA Multicenter Prehosptial Hemoglobin-based Oxygen Carrier Resuscitation Trial: Scientific Rationale, Study Design, and Results

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KEYWORDS

• Hemoglobin-based oxygen carrier • Blood substitute
• Prehospital resuscitation • Hemorrhagic shock • Trauma

The current generation of blood substitutes tested in clinical trials are red blood cell (RBC) substitutes; that is, they are designed primarily to transport oxygen. The products now being used in advanced-phase clinical trials are derived from hemoglobin (Hb) and are thus often referred to as Hb-based oxygen carriers (HBOCs). The potential benefits of HBOCs are well known (**Box 1**). The objectives of this overview are to provide the scientific background and rationale for the study design of the USA Multicenter Prehospital HBOC Resuscitation Trial and to present the results and discuss clinical implications.

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Box 1
Potential clinical benefits of hemoglobin-based oxygen carriers in trauma care

Availability
Abundant supply
Universally compatible
Prolonged shelf-life
Storage at room temperature
Safety
No disease transmissions
No antigenic reactions
No immunologic effects
Efficacy
Enhanced oxygen delivery
Improved rheologic properties

POTENTIAL ROLE OF HEMOGLOBIN-BASED OXYGEN CARRIERS IN TRAUMA CARE

The US Food and Drug Administration (FDA) approval of a new product proceeds through phase I, II, and III studies designed to establish safety and efficacy (**Table 1**). FDA regulation defines efficacy as follows: ''Effectiveness means a reasonable expectation that…the pharmacologic or other effect of the biologic product…will serve a clinically significant function in the diagnosis, cure, mitigation, treatment, or prevention of disease in man.''[1] The Center for Biologics Evaluation and Research (CBER) is the review body for the FDA in the arena of biologies and has published a comprehensive listing of ''points to consider in the safety evaluation of HBOCs.''[2]

Table 1
Potential role of hemoglobin-based oxygen carriers in trauma care

Application	Location
Perioperative applications	
Reduce allogeneic RBC transfusions	ED, angiography, OR, ICU
Attenuate transfusion immunodulation	OR, ICU
Acute hemorrhagic shock	
When stored RBCs are unavailable	Field, ED, OR, ICU, remote hospital, civilian disaster, military conflict
More efficient resuscitation	Field, ED, OR, ICU
Low-volume resuscitation	Remote hospital, civilian disaster, military conflict
Regional perfusion	
Enhance oxygen delivery	
Ischemic reperfusion tissue/organ	OR, ICU
Inflamed tissue	OR, ICU
Ex vivo organ perfusion	Hospital, OR

Abbreviations: ED, Emergency department; OR, Operating room.