

POLYHEME® TRAUMA TRIAL FREQUENTLY ASKED QUESTIONS AND ANSWERS

Why is this study being conducted?

To evaluate the safety and efficacy of PolyHeme® in treating severely injured and bleeding patients, starting at the scene of injury, and to assess a potential survival benefit.

What is the title of this study?

A Phase III, Randomized, Controlled, Open-Label, Multicenter, Parallel Group Study Using Provisions for Exception from Informed Consent Requirements Designed to Evaluate the Safety and Efficacy of Poly SFH-P Injection [Polymerized Human Hemoglobin (Pyridoxylated) PolyHeme®] When Used to Treat Patients in Hemorrhagic Shock Following Traumatic Injuries Beginning in the Prehospital Setting

What is the design of this study?

Patients in “hemorrhagic shock” will begin to receive either saline (salt water), which is the standard of care (control), or PolyHeme (investigational treatment). Treatment would begin before arrival at the hospital, either at the scene of the injury or in the ambulance, and continue during a 12 hour postinjury period in the hospital.

In the hospital, patients in the control group will receive saline for hydration and blood if necessary to boost oxygen levels. Unlimited doses of each are allowed.

Patients in the treatment group will receive saline (salt water) for hydration and PolyHeme® to boost oxygen levels if necessary. The maximum dose of PolyHeme will be 6 units during the first 12 hours. Blood will be used thereafter.

What is hemorrhagic shock?

A condition in which a patient has experienced massive blood loss. Shock is a life-threatening condition that might include:

- Dangerously low blood pressure
- Internal organs not receiving enough oxygen and have difficulty functioning, which could lead to death

Why is there a need for improvement in the way trauma patients are treated now?

Trauma is the leading cause of death among Americans under the age of 45. Currently the only available treatment for hemorrhagic shock, when blood is not available, is the infusion of a solution such as saline, which does not carry oxygen. Therefore, when blood is not immediately available, use of an oxygen carrier such as PolyHeme may restore sufficient circulating levels of hemoglobin and potentially improve patient survival.

What is the current standard of care? How are trauma patients usually treated?

Patients are given a solution such as saline at the scene or in the ambulance. When they arrive at the hospital, they are given blood after typing and cross matching is accomplished.

Who would be eligible for the study?

Patients who have lost a large amount of blood and are in shock
Patients who are at least 18 years old
Patients who have sustained severe injuries

Who would be excluded from the study?

Women who are obviously pregnant
Patients with severe brain injuries
Patients who require CPR to maintain their heartbeat
Patients with "unsurvivable" injuries
Patients who are known to object to blood transfusions
Patients who are known to refuse resuscitation

What is PolyHeme®?

PolyHeme® is an oxygen-carrying blood substitute made from human blood. PolyHeme® requires no cross-matching, and therefore is compatible with all blood types. It could provide immediate therapy when blood is not available. PolyHeme® is highly purified to reduce the risk of viral disease transmission. It has a shelf-life of over 12 months.

Has PolyHeme® been tested on humans before?

There have been 5 human clinical trials of PolyHeme®.

The observations in these trials have demonstrated the potential usefulness of PolyHeme in the treatment of urgent blood loss and life-threatening hemoglobin levels. In these trials of hospitalized patients, PolyHeme significantly improved survival compared to historical control patients who did not receive blood. The trials have involved high dosage and rapid infusion of PolyHeme in situations that are life-threatening and where massive blood loss routinely occurs.

How many patients have been treated with PolyHeme®?

Over 300 patients have been treated, including patients in a hospital-based trauma trial.

What is known about the safety of PolyHeme®?

PolyHeme® has been demonstrated to be well tolerated in the patient populations tested in clinical trials to date.

What is an exception from informed consent?

Patients are enrolled in a clinical study without giving informed consent before being enrolled.

Why was such an exception granted in connection with this study?

Patients are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence is necessary to determine the safety and effectiveness of particular interventions.

Participating in the study has the potential for of direct benefit to the enrolled patients, defined as an increase in survival, because:

- Patients are in a life-threatening situation that necessitates intervention
- Previous studies support the potential to provide a direct benefit to enrolled patients
- Risks associated with the use of the PolyHeme® are reasonable in relation to what is known about the patients' medical condition, the risks and benefits of standard therapy, and the risks and benefits of the proposed intervention

It is expected that patients will be unable to give informed consent because the extent of their injuries and the fact that they are in shock.

It is unlikely that there will be time to find and ask for consent from the patient's legally authorized representative (LAR) or to provide an opportunity for a family member to object to the patient's enrollment before beginning treatment.

Who grants such exceptions?

The U.S. Food and Drug Administration (FDA) under regulations called 21 Code of Federal Regulations 50.24 specifies the conditions under which an exception from informed consent may be obtained. The Institutional Review Board (IRB) associated with each hospital approves its use locally.

What if patients don't want to participate in this study?

Patients can withdraw from the study, without prejudice, at any time by notifying the investigator.

Will patients still receive treatment if they don't want to participate in the study?

Patients will still receive the standard of care if they decline to participate in this study.

What are the potential benefits of participating in the study?

PolyHeme® may increase the likelihood of survival after traumatic injury

The need for blood transfusion might be reduced

Patients might avoid a reduction in the function of internal organs that sometimes follows blood transfusion.

What are the potential risks of participating in the study?

Rash
Increased blood pressure
Kidney or liver damage
Transmission of hepatitis and HIV viruses
Unforeseen happenings

How much will it cost patients to participate?

There is no charge to the patient to participate in this study. The costs of certain laboratory tests that are required will be paid by the study sponsor.

Will patients get paid to participate?

No, patients will not be paid to participate in this study.

Who is the manufacturer of PolyHeme®?

Northfield Laboratories Inc., Evanston, IL. For more information, visit www.northfieldlabs.com