UNIVERSITY OF WASHINGTON

Information sheet to accompany Consent for continued participation

A Prospective Randomized Prehospital Trial Comparing Kcentra plus Standard of Care to Placebo plus Standard of Care in Trauma Patient with Hemorrhagic Shock

The purpose of this document is to provide you with information about the research that occurred prior to asking for your consent to participate.

PURPOSE OF THE STUDY

The purpose of this study is to learn about a medicine that may help people with traumatic injuries who may require blood products to help control or stop bleeding.

Emergency treatment is given to people with serious bleeding injuries to help the body make blood clots or promote blood flow to vital organs such as the brain, heart, lungs, and kidneys. The body quickly responds to traumatic injuries by forming blood clots inside the damaged blood vessels to stop the bleeding. The blood clot may be able to stop the blood from leaking out of the damaged blood vessel.

The first priority of medical treatment is to help the body make blood clots that stop the bleeding. Paramedics use measures to help clots form such as applying direct pressure to a surface wound or applying a tourniquet (an elastic cord used to compress blood vessels when tightened by twisting) above a wound on an arm or leg. If the bleeding is inside the chest, abdomen (belly), or pelvic (lower belly) area, surgery performed in a hospital may be the only effective method to stop the bleeding. An injured person at risk for bleeding that cannot be stopped by direct pressure or a tourniquet needs to be taken to a hospital as soon as possible.

If the amount of blood lost is too large, vital organs such as the brain, heart, lungs, and kidneys will not receive the blood they need to function properly. In these cases, many people need blood products such as plasma to promote blood clotting. However, because of storage requirements, most paramedics aren't able to carry plasma on their vehicles. A drug called Kcentra, which is a four-factor prothrombin complex concentrate, is often used to promote clotting in people who need to reverse the result of taking blood thinners. We believe it may also be helpful to patients who are bleeding due to their traumatic injuries.

When medics determined injuries were serious and potentially life-threatening, a decision was quickly made to enroll you in this study and start study treatment before you got to the hospital. This is because the study investigators believe the study drug needs to be started quickly in order to be effective. Special permission has been granted by our review board here, the University of Washington Institutional Review Board (IRB) and the Food and Drug Administration (FDA) to enroll subjects in this study without their prior consent due to the emergency nature of their injury. The IRB and FDA oversee the safety of subjects in medical research.

Because of your injuries, we were unable to talk to you before you were enrolled into this study. In cases where we are not able to get permission (consent), we will include the injured person in the study using a Food and Drug Administration (FDA) approved process for emergency situations called Exception from Informed Consent Requirements for Emergency Research (EFIC). We will continue to try to get consent, even after we have included an injured person in the study.

Each of the local hospitals likely to admit patients with a severe trauma have also approved this study, including Harborview Medical Center. The Food and Drug Administration (FDA) reviewed this study.

Additionally, a Data Safety Monitoring Board, was chosen to monitor the results of the research during the course of the study to be sure of patient safety. Only after this process was done could the study start.

This study will enroll 166 subjects across the United States. The study will enroll approximately 60 subjects here in the Seattle area.

STUDY PROCEDURES

If you agree to continue in this study, your medical and surgical care will not be changed. You were enrolled in this study by the medics who first cared for you and brought you to the hospital. After providing you with needed emergency care, medics observed physical symptoms of traumatic injury that made you eligible for this study. They then enrolled you in the study and gave you either Kcentra or a placebo through a vein in your arm (IV). The placebo is it is a foamy, volume matched fluid with non-active components of Kcentra

The package of study medication was designed so that the medic and hospital staff do not know which dose of study drug you received or if you received placebo. This is called "blinding." Kit numbers containing study drug or placebo are assigned randomly, like flipping a coin. Neither you nor the investigator can choose whether you get study drug or the placebo. The study is done this way because knowing whether you are getting the study drug can change the results of the study. If you start having serious side effects from the study drug, the investigators can find out what you were given in order to help you. Please ask the investigator if you have any questions at all about this kind of study. Study treatment is done in addition to all regular care.

Blood samples for research testing (about 2 tablespoons each) are collected on arrival to the hospital and at 2, 12, 24, 48, 72, and 96 hours. The blood samples for this study will be used to look at how your blood is clotting (or clumping together).

RISKS, STRESS, OR DISCOMFORT

You may have some side effects we do not expect because we are still learning about Kcentra.

You may not have symptoms for some of these side effects, but you will be monitored by the investigator to check for any changes throughout the study.

One risk to taking part in this study is that the study drug or the dose you receive may not be effective in helping to treat your injuries. This means you may spend time in the study and experience side effects taking a drug that may not provide you with any health-related benefits.

The most common adverse reactions (occurring at frequency $\geq$ 2.8 %) observed in patients receiving Kcentra are:

- Headache
- Nausea/vomiting
- Arthralgia (joint pain)
- Hypotension (low blood pressure)

The most serious adverse reactions associated with Kcentra are:

- Allergic reaction that could cause rash, fever, vomiting, swelling, dizziness or difficulty breathing
- Blood clots that could block blood flow to vital organs such as the heart, kidneys, lungs and brain. This could cause a heart attack, kidney failure, difficulty breathing or stroke and lead to death if not treated right away.
- Possible transmission of infectious agents
- Embolic cerebral infarction

- Increased body temperature
- Myocardial ischemia
- Anaphylactic reactions

If you are nursing an infant or you are pregnant now, you must not be in the study. This study may involve risks to an embryo, fetus, or nursing infant that are currently unknown. If you are suspected or known to be pregnant at the time of injury, you will not be enrolled in the study. It is possible that pregnant women will be enrolled and receive study drug if the medics are not aware of the pregnancy. If pregnancy is confirmed in the Emergency Department, you will be followed for safety. If the pregnancy is confirmed after the study drug has been started, the study drug will be stopped because we do not know if it is harmful to pregnant women or their developing fetus.

BENEFITS OF THE STUDY

You may not directly benefit from this study. We cannot guarantee that there will be any benefit to you. The study may determine there is no benefit from receiving Kcentra. It is not yet known that Kcentra provides a benefit. All patients who participate in this trial will have the potential to benefit. Subjects who receive Kcentra may benefit by having bleeding controlled sooner.