CRYOSTAT-2
EARLY CRYOPRECIPITATE IN TRAUMA

IRAS Reference no: 210735

INSERT HOSPITAL LOGO

Patient and Personal/Nominated Consultee Information Sheet

Title of Study: A multi-centre, randomised, controlled trial evaluating the effects of early high-dose cryoprecipitate in adult patients with major trauma haemorrhage requiring major haemorrhage protocol (MHP) activation.

Chief Investigators: Professor Karim Brohi, Dr Simon Stanworth

Sponsor: Queen Mary, University of London (QMUL)

Introduction

This hospital is taking part in a research study to investigate a treatment for bleeding in patients with serious injury. You are being asked for your:

1. **Consent (if you are the patient):** You recently suffered from a severe injury and major bleeding and were admitted to hospital. As part of your emergency care you received the standard major haemorrhage therapy which is used at this hospital to treat people with severe injuries and bleeding. The doctors treating you agreed that you were eligible for a study to investigate a treatment for bleeding in patients with severe injuries and enrolled you to the study. The decision was made by your doctors on your behalf as you were too unwell to consider taking part at that time. Now that your condition has improved, we would like to give you more information about the study and ask you whether you would like to consider continuing in the study.

2. **Advice (if you are the patient's personal/nominated Consultee):** We are asking your opinion of the patient's wishes or feelings as to whether to continue to participate in this study. You are free to decide whether you wish to make this decision or not. Take time to decide whether or not you wish (the patient) to continue to participate in this research study.

   Please let us know of any advance decisions they may have made about participating in research. These should take precedence.

   If you decide your relative/friend would have no objection to continuing to take part we will ask you to read and sign the consultee declaration. We will keep you fully informed during the study so you can let us know if you have any concerns or you think your relative/friend should be withdrawn. If you decide that your relative/friend would not wish to take part it will not affect the standard of care they receive in any way.

   If you are unsure about taking the role of consultee you may seek independent advice. We will understand if you do not want to take on this responsibility

This research will help us improve the care of patients who suffer severe injuries in the future. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information.

Key Facts about this Study

- The doctor decided that on admission to hospital you (the patient) needed emergency treatment which included the 'standard major haemorrhage therapy'. This is blood transfusion therapy, which includes red blood cells, fresh frozen plasma, platelets and cryoprecipitate and is routine treatment for major bleeding. Usually, the major haemorrhage therapy is

administered to patients with severe injuries and major bleeding very soon after admission to hospital.

- Fibrinogen is an important blood molecule which is key to the formation of blood clots, which we know helps to stop active bleeding.
- In severe injury and major bleeding, levels of fibrinogen in the blood may fall quickly and this can make the bleeding more severe.
- In this study we are investigating a blood transfusion product rich in fibrinogen called cryoprecipitate, which is already given to patients as part of the routine treatment for major bleeding.
- We believe that giving cryoprecipitate as quickly as possible to patients admitted to hospital will improve their fibrinogen levels and potentially stop the bleeding quickly.
- Cryoprecipitate has been used clinically for over 40 years and has a good safety profile.
- Our ultimate aim is to show that giving cryoprecipitate as quickly as possible will improve survival in patients with severe injury and major bleeding.
- You (the patient) were eligible to participate in this study when you needed the standard major haemorrhage therapy as treatment for major bleeding.

What is the purpose of this study?

Worldwide, injury accounts for 5.8 million deaths every year, equivalent to one death every nine minutes and it is the leading cause of death in people under the age of 44. Bleeding accounts for 40% of all injury-related deaths. Transfusion therapy is an important part of emergency treatment for major bleeding. In our previous small study, it was shown that early replacement of fibrinogen with cryoprecipitate was able to rapidly restore fibrinogen levels and may reduce deaths from bleeding.

The main aim of this study is to test whether giving cryoprecipitate (within 90 minutes of admission), during major bleeding after trauma will reduce the number of deaths reported. This study will involve approximately 1568 patients admitted to hospitals across the UK and other countries such as the USA.

In this study, one group of patients who take part in the study will be given cryoprecipitate early (3 pools equivalent to 6g of fibrinogen) as well as the standard major haemorrhage therapy. The other group of patients taking part will be given only the standard major haemorrhage therapy.

The effects of the two different treatments will be compared by assessing the patients' rates of death in the two groups which will tell us whether giving cryoprecipitate earlier can improve survival. We are also investigating the quality of life that patients have.

Why have I been invited to take part?

You (the patient) are being asked to continue to participate in this research study because you were admitted to the hospital with severe bleeding. On arrival to hospital you needed immediate treatment with major bleeding therapy and you were deemed to be eligible for this study. You were too unwell to make a decision about participation at the time of admission. You are now being asked if you will consider continuing in this study.

What will happen to me if I agree to continue to take part?

You (the patient) have already been randomly allocated in to one of two groups of the study. One group received an early dose of cryoprecipitate (6g fibrinogen) with standard major haemorrhage treatment. The other patient group received the standard major haemorrhage treatment alone. The group you are in was determined randomly and there was a 50/50 chance of being in either group.

During your stay in hospital, we will review your progress. We will record information about other illnesses if they occur. You will not need to give extra blood samples for taking part in this study.

As part of a UK wide project, the Trauma Audit & Research Network (TARN), routinely ask patients admitted to hospital with major bleeding after injury to complete questionnaires which asks patients about how they feel about their health. During your hospital stay (either at discharge or at a month of being in hospital) you may be asked to complete this questionnaire by a member of the research team. If you completed a questionnaire in hospital, six months following your admission you will be contacted by TARN to complete the same questionnaire.

We would also like to follow up how patients are doing for up to one year following their hospital admission and record any deaths and causes of death that may have occurred in that period. For this reason we will be accessing centralised mortality (death) data captured by the Office for National Statistics (ONS) which is held by NHS Digital.

We will seek your signed informed consent to use your identifiable information to obtain data from TARN and NHS Digital. Your information will be stored securely on a password protected NHS servers by NHS Blood & Transplant, accessible only by the research team. We have permission to share your/your loved ones' identifiable information in certain circumstances without signed informed consent. At the end of this study, all identifiable data stored will be destroyed.

If for any reason we are unable to follow you up remotely then a member of the research team may contact your GP or you directly.

What are we testing in this study?

We are testing whether giving cryoprecipitate early (within 90 minutes of a patient being admitted to hospital) following a major injury, can reduce bleeding and death.

What are the possible benefits of taking part?

There is no known direct benefit from participation in this study at the present time. Participants receiving early administration of cryoprecipitate might respond better, but at present we do not know if this will be the case.

What are the possible disadvantages and risks of taking part?

All the blood products that will be used in the CRYOSTAT 2 study have been approved for use in the UK and have been treated for viruses and other pathogens according to normal procedures. Cryoprecipitate has been used clinically for over 40 years and has a good safety profile. There is a small chance that patients receiving cryoprecipitate early may raise their blood fibrinogen level higher than those receiving standard care and this may increase the risk of clots such as deep vein thrombosis (DVT), clots in the lungs, heart attacks and strokes. However, in small trauma studies to date there has been no evidence of an increased risk of developing clots. As far as we know, there are no additional risks associated with participating in this trial.

Safety events will be reviewed periodically by an independent Data Monitoring Committee who will advise if there are any safety concerns during the study.

What if there is a problem?

If you have any concerns about any aspect of this study, you should ask to speak to the researchers who will do their best to answer any questions. If you remain unhappy and wish to complain formally, or if you wish to speak to someone who is independent of this study please contact your local hospital **Patient Advice and Liaison Service (PALS) on [enter telephone number here].**
In the unlikely event that you suffer injury as a result in taking part in this research, the University does have an insurance policy to cover harm arising as a result of the defect in the design of the study. Compensation for any injury caused by taking part in this study will be in accordance with the guidelines of the Association of the British Pharmaceutical Industry (ABPI). Broadly speaking the ABPI guidelines recommend that the "sponsor" (QMUL) without legal commitment, should compensate you without you having to prove that it is their fault. This applies in cases where it is

likely that such injury results from giving any new drug or any other procedure carried out in accordance with the protocol for the study. The "sponsor" (QMUL) will not compensate you where such injury results from any procedure carried out which is not in accordance with the protocol for the study. Your right at law to claim compensation for injury where you can prove negligence is not affected

What will happen if I don't want to carry on with the study?

It is up to you to decide whether to take part in the research or not. If you decide to continue to take part you will be free to change your mind at any time, without giving a reason. If you did decide to withdraw from the study at any time it will not affect the standard care you receive now or at any time in the future. If you agree to continue to take part in this study, you will be given this information sheet to keep and will be asked to sign a consent form.

If you do withdraw from the study, we will aim to use the data we have collected up to your withdrawal, or if you prefer we can destroy all information so that you will be completely removed from the study.

We would like to continue to monitor you for safety, which may mean the study team will wish to contact you.

Will my taking part in the study be kept confidential?

Queen Mary University of London (QMUL) is the Sponsor for this clinical trial which is based in the United Kingdom and has delegated overall management of this study to the Clinical Trials Unit at NHS Blood & Transplant, and will act as joint data controllers. This means that we are responsible for looking after your information and using it properly.

Your information will only be used by researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research**.**

We will be using information from you and your medical records in order to undertake this trial.

As publicly-funded organisations, we have to ensure that it is in the public interest when we use personally-identifiable information from people who take part in research.

We will keep identifiable information about you for 2 years after the study has finished to allow us to complete analysis of the data that we have collected. After this time your identifiable information will be deleted.

To safeguard your rights, we will use the minimum amount of personally-identifiable information possible.

The personally-identifiable information we will collect are: Name, date of birth, sex, NHS number (or CHI number if you live in Scotland) and postcode. This data is shared with NHS Digital so that we can check on your survival status one year after your injury. We will also access information collected by the Trauma Audit & Research Network (TARN, hosted by the University of Manchester) about how you feel about your health. By accessing existing TARN data, it means that we do not need to ask you for the same information twice. NHS Blood & Transplant will have a contract with NHS Digital and The University of Manchester that ensures the security and integrity of your data at all times.

You have the right to access, correct or complete the information you have given us. You also have the right to withdraw from the trial at any time and request that your data be deleted ("right to be forgotten"). If you wish to withdraw, please arrange to speak with the doctor or nurse listed at the bottom of this patient information sheet.

After the trial has been completed, we will provide QMUL with an anonymised data set produced by the research. This information will not identify you and cannot be combined with other information in a way that could identify you.

You can find out more about how we use your information in research at https://www.hra.nhs.uk/information-about-patients/ or by contacting the Trial Manager by email at cryostat2@nhsbt.nhs.uk

Under GDPR, all NHS organisations are legally required to appoint a Data Protection Officer (DPO). The DPO for NHS Blood & Transplant is Aaron Powell, the Chief Digital Officer, who is responsible for ensuring that all practices and processes within NHS Blood & Transplant are designed to support people's privacy and data rights. You can contact the DPO by email at dpofficer@nhsbt.nhs.uk

You can also look at the website of the Information Commissioner (https://ico.org.uk/) for more information on the new GDPR legislation and you have the right to speak to them if you are worried that your data is not being appropriately protected or processed.

Will my GP be informed of my participation in the study?
Yes, we will write to your (the patient) general practitioner/family doctor to tell him/her about the study and inform him/her that you are taking part.

What will happen to the results of the study?
Once the study is completed the results will be published in Scientific and Medical Journals and presented at meetings of health professionals. We will also provide a summary of the results on a dedicated CRYOSTAT 2 website which can be accessed from: www.nhsbt.nhs.uk/clinicaltrialsunit. You (the patient) will not be identifiable in any publications or presentations resulting from this study.

Who is organising the research and why?
The study is being managed by Investigators at NHS Blood and Transplant, and the Centre for Trauma Sciences, Queen Mary University of London. The study is funded by the NIHR Health Technology Assessment programme.

Who has reviewed the study?
All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by South Central – Oxford C Research Ethics Committee.

Who should I contact for further information?
If at any time during the study you have questions or concerns regarding the study you can contact the local Principal Investigator or Research Nurse, who is in charge of the research study at your hospital:

Principal Investigator name/ contact details_____

Research Nurse name/ contact details_____

Thank you for taking the time to consider continuing to take part in the CRYOSTAT-2 study.