Queen Mary University of London

Barts Health NHS Trust

The TOP-ART Study: Trauma Organ Protection: Artesunate

Participant Information Sheet

DIRECTORATE OF SURGERY AND ANAESTHESIA
ROYAL LONDON HOSPITAL
BARTS HEALTH NHS TRUST

Version 1.0
Ethics Committee
REC number XXXX

Title of Study: A randomised blinded, placebo-controlled Phase 2a study to evaluate the safety and efficacy of Artesunate treatment in severely injured trauma patients with traumatic haemorrhage.

Short Title: TOP-ART

Principal Investigator: *Professor Karim Brohi, FRCS, FRCA*

Sponsor: Queen Mary University of London

Date: ___/___/_____

Subject Name: _____. NHS Ref: _____ Study Ref: _____

PART 1

Introduction

You are being asked to provide consent to continue participating in a research study. This research may help us to 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. Talk to others about the study if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to continue to participate in this study.

Key Facts about this study

- You recently suffered from a severe injury and were admitted to hospital.
- Patients that sustain severe injuries particularly with major blood loss are at increased risk of developing multiple organ failure, which can result in worse outcomes.
- Laboratory studies suggest that Artesunate, a medication that is routinely used for treating malaria, may help protect organ function in severe injury and bleeding, and therefore improve outcomes.
- This research project, the TOP-ART trial, is designed to test if administering Artesunate to patients who sustain major injuries is safe, and to make some preliminary judgements about whether this improves patient outcomes by reducing the risk of multiple organ failure.
- You were eligible to participate in this trial due to the severe nature of your injuries. The doctors decided to enter you into the study because you were too ill to make a decision about participation.
- We are approaching you now to ask for your consent to continue to participate in this study

What is the purpose of this study?

Trauma (serious injury) is the leading cause of death and disability in children and young adults worldwide. It is estimated that almost one in three patients who sustain severe injuries develop multiple organ failure. This condition can result in worse outcomes such as longer intensive care and hospital stays, poor long-term quality of life, and higher chance of death. Worsening shock and degree of blood loss are associated with increased likelihood of developing multiple organ failure.

Currently there are no specific treatments for multiple organ failure. However, laboratory studies suggest that a medication called Artesunate may reduce the risk of developing multiple organ failure and therefore improve outcomes in severely injured patients. The World Health Organisation

recommends Artesunate for the treatment of malaria (the usual dose is 2.4mg/kg every 12 hours). The medication has been used on thousands of people worldwide without important adverse effects.

The main objective of this clinical trial is to test whether Artesunate administered in addition to the standard medical treatment is safe and effective in reducing the risk of organ failure in patients who sustain major injuries. To find out if Artesunate is effective, participants in this trial have either been administered a single dose of Artesunate (the study medication) or a placebo (which containins no active ingredient and therefore has no effect on outcomes) in addition to standard medical treatment.

In order to identify the optimal dose of Artesunate, the trial has been divided into two stages:
Stage 1: Participants who received a standard dose of Artesunate (2.4 mg/kg) or Placebo.
Stage 2: Participants who received a higher dose of Artesunate (4.8 mg/kg) or Placebo.

We do not expect to have any safety concerns with administering Artesunate at these doses. The reason for using a higher dose is that our laboratory studies suggest it may be more effective than the standard dose in preventing organ failure in trauma. Stage 2 of the study only takes place after an analysis of Stage 1 participants shows no safety concerns with the medication.

Why have I been invited to take part?

On ___ - ___ - _____ (date), you were injured and admitted to the Royal London Hospital. At the time, you were unable to give informed consent. When you arrived in the emergency department, a full trauma team of doctors and nurses attended to you. The trauma team leader, who is not part of this research study, gave consent as your representative for you to be enrolled in this study. We are now asking for your consent to continue to participate in the study.

What treatment have I already received?

In addition to your standard medical care, you have received a dose of either Artesunate or Placebo. This was administered intravenously within the first two hours of your admission. You have been entered into Stage _____ of the trial, meaning that you have received _____mg/kg of Artesunate or Placebo.

We determined whether to administer Artesunate or Placebo using a random allocation schedule that was produced before the trial started. You are twice as likely to have received the Artesunate medication rather than Placebo. We cannot tell you whether you received Artesunate as the trial is blind – this means that the participant and the clinicians responsible for their care do not know which

preparation was given until the end of the study. This is to avoid having any unintentional impact on the results of the trial.

What procedures have already taken place?

In order to measure the levels of trial medication in your blood, a small amount of blood was drawn at set time intervals during the first 12 hours of the trial medication being administered (a maximum of six samples). Each sample contains up to 2 teaspoons of blood. A total of _____ blood samples were taken from you for this purpose. These samples were stored and will be sent to a laboratory that specialises in measuring levels of Artesunate in blood.

In order to ensure that the drug has not had any adverse effects, we also check the results of blood tests that are taken by the clinical team. This includes results that tell us about your red and white blood cells, and your kidney and liver function. We record these blood tests daily during the first week of admission, and weekly for the following 3 weeks (a maximum of 10 samples, each containing up to 2 teaspoons of blood). Most of these blood tests are taken routinely as part of your medical management; however, occasionally this is done as an extra trial blood test. We have already taken _____ blood tests for this purpose.

Do I have to continue *to* take part?

No, participation is completely voluntary. It is up to you to decide whether or not to continue to take part. If you agree to continue to participate in this study, you will be given this information sheet to keep and asked to sign a consent form. You are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

What will happen next if I agree?

During your stay in hospital, we will review your progress to see how your organs are functioning. We will record information about other illnesses if they occur and about how long you stay in the intensive care unit and in hospital overall. With your permission, we will also inform your General Practitioner (GP) of your enrolment in the study.

In order to continue to monitor the trial medication levels in your blood, we will take a further _____ blood samples at:

_____(dates/times)

In order to continue to follow you up for adverse effects of the trial medication, we will take a further _____ blood samples at:

_____

_____(dates/times)

If you are discharged before 28 days in hospital, we may need to contact you or your General Practitioner to enquire if you have experienced any adverse medical events following your discharge. We will also check your NHS records at 90 days following your enrolment.

What are the possible disadvantages and risks of taking part?

Artesunate is generally well tolerated, however there is a very small risk that if you receive this medication you may develop an adverse reaction. The most common side effects include: gastro-intestinal symptoms (e.g. nausea, vomiting, abdominal cramps, bitter taste), nervous system symptoms (e.g. dizziness, headache, insomnia), skin symptoms (e.g. rash, itching), and general symptoms (e.g. fatigue, joint pain). The trial medication can cause derrangements in your blood tests, including anaemia and transient derrangements in your liver enzymes, however these are uncommon. The chance of a severe allergic reaction is very rare (approximately 1 in 3000). We will monitor you for adverse reactions during your hospital admission. If you receive the placebo preparation, there will be no added risks.

With regards to blood sampling, there are no serious risks to your health. Specific risks include temporary discomfort from the needle stick and bruising.

What are the possible benefits of taking part?

There is no direct benefit from participating in this study at the present time. Based on our laboratory studies, participants who are administered Artesunate may have a reduced risk of developing of multiple organ failure. If the results of this study suggest that Artesunate is effective, then this research will help in designing a larger clinical trial to confirm this finding. If proven to be effective, these studies could lead to Artesunate being incorporated into standard medical treatment of patients who sustain major injuries.

What if there is a problem?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

Will my taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

This Completes Part I.

If the information in Part 1 has satisfied you and you are considering continuing in the study, please read the additional information in Part 2 before making any decision.

PART 2

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

If you decide, at any time, to withdraw from the study all study procedures will be stopped immediately. Any information and samples that have already been collected will be processed as part of the study unless you wish to have your samples withdrawn from the study, in which case we will destroy them. Your decision will in no way result in a change in the type or quality of care you subsequently receive.

What if I am not happy about the study?

Apart from receiving Artesunate or the placebo following your admission to hospital, you will receive normal clinical care. It is unlikely that adding this medication to the normal clinical care you receive will cause any problems. However, if you are harmed by taking part in this study, there is no special compensation arrangement. If you are harmed due to someone's negligence, then you may have grounds for legal action but you may have to pay your legal costs.

Regardless of this, if you wish to complain or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms should be available to you. Please contact Patient Advisory Liaison Service (PALS) if you have any concerns regarding the care you have received, or as an initial point of contact if you have a complaint. Please telephone 020 3594 2040, or email pals@bartshealth.nhs.uk . You can also visit PALS by asking at any hospital reception.

Will my taking part in the study be kept confidential?

All information which is collected about you during the course of the research will be kept strictly confidential and will be stored securely in coded form. Information about you and your samples will be identifiable only in a coded format, separate from your personal information. Only authorised personnel such as researchers and research auditors will have access to the data.

What will happen to your study data and samples?

Your study data and samples (i.e. materials) will always be collected, stored, transferred and used in a secure and ethical manner that ensures protection of your fundamental rights and privacy.

All materials will initially be processed at the research centre where you were enrolled and linked to you by a unique study identifier (i.e. coded). Your blood samples will be transferred to a research unit specialised in measuring Artesunate levels (Mahidol Oxford Tropical Medicine Research Unit,

Bangkok). Study materials will not be able to be linked back you, other than by responsible personnel at the site of your original enrolment. The coded data and samples will only be accessed by authorised personnel (e.g. research fellows, study auditors).

We will not share your personal details (e.g. name, address). Necessary key personal information may be retained for analysing the trial results (e.g. age, gender, clinical and treatment data) but all study information will be anonymised at the end of the trial when results are published. We hope that this trial will allow us to identify new areas of investigation and potentially allow future trauma care to be specifically tailored to the characteristics of each individual patient.

What will happen to the results of the research study?

We hope to publish the results in a scientific journal. It will not be possible to identify any individual who has taken part from this scientific report. Copies of the report will be available on request.

Who has reviewed the study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee to protect your safety, rights, wellbeing and dignity.

This study has been reviewed and given favourable opinion by East London & City Research Ethics Committee 1.

Who can I contact for further information?

1. If you require further information about the study, please contact the Artesunate Trial researchers by telephone: 020 3594 0731 or by email: c.rourke@qmul.ac.uk or Joanna.Shepherd@bartshealth.nhs.uk
2. If you require impartial, local advice, please contact the Patient Advice and Liaison Service, telephone: 020 3594 2040 or e-mail: pals@bartshealth.nhs.uk.

Thank you for taking the time to read this information.

Date: ___/___/_____ Researcher Signature: _____ _____