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The TOP-ART Study: Trauma Organ Protection - Artesunate

Submission date	Recruitment status
25/08/2015	No longer recruiting
Registration date	**Overall study status**
28/08/2015	Completed
Last Edited	**Condition category**
10/05/2021	Injury, Occupational Diseases, Poisoning

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Major trauma accounts for a significant number of deaths worldwide, and is one of the most frequent causes of death in people under the age of 40. A large number of these deaths are caused by massive blood loss (haemorrhage). Low blood pressure due to blood loss puts extreme pressure on vital organs such as the heart and brain, as they are not receiving enough oxygen. Without correct treatment, this eventually leads to multiple organ failure (MOF). Development of MOF occurs early (within two days of admission) and is related to an increase in hospital-acquired infections and even death. There is currently no specific treatment which is used to protect against MOF after traumatic haemorrhage however. Artesunate is a drug that has been used for many years as the treatment of choice for severe malaria. It has very few adverse effects and can even be used safely for patients suffering with liver or kidney disease. Laboratory experiments using animals have shown that this drug can actually reduce the risk of organ failure after haemorrhage, as it enhances the protection of organs within the body. This study aims to test the safety and effectiveness of the use of Artesunate in patients with severe trauma and blood loss.

Who can participate?
Adult trauma patients who are actively bleeding as the result of traumatic injury.

What does the study involve?
Due to the urgent/emergency nature of the intervention subjects are recruited within 4 hours of their injury and within 2 hours of admission to the Emergency Department. All participants receive emergency care in accordance with local guidelines for traumatic haemorrhage. Patients are randomly allocated into one of three study groups, receiving either low dose Artesunate (2.4mg/kg), high dose Artesunate (4.8mg/kg) or placebo (inactive medication). Artesunate is given intravenously (though a vein) because the critical condition of the patients means that it is not an option to take the drug orally. Each participant is given the drug, and then remain in the study for 28 days or until they are discharged from hospital. A scoring system known as the Sequential Organ Failure Score (SOFA) is used throughout this period, in order to track the rate of organ failure in the patients.

What are the possible benefits and risks of participating?
The potential benefits of Artesunate in reducing multiple organ failure outweigh the risk of adverse events associated with the medication. Artesunate has been extensively used in the treatment of both child and adult malaria, including use in critically ill patients. As patients will receive all other clinically indicated treatments, there is no risk of ineffective therapy by administration of the study treatment.

Where is the study run from?
The Royal London Hospital (UK)

When is the study starting and how long is it expected to run for?
April 2015 to September 2019

Who is funding the study?
Wellcome Trust (HICF-R7-405) (UK)

Who is the main contact?
Ms Claire Rourke (Public)
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Study website
http://www.c4ts.qmul.ac.uk/organ-failure--protection/top-art

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
2015-000301-40

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
REDA 009531 / 1.0

Study information

Scientific Title
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.

Acronym
TOP-ART

Study objectives
The aim of this study is to determine whether treatment with Artesunate improves the outcome in severely injured subjects with trauma haemorrhage.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London - City & East Research Ethics Committee, 11/03/2016, ref: 16/LO/003

Study design
Single-centre randomized placebo-controlled parallel group study with a sequential group-dosing regimen (adaptive design).

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet.

Health condition(s) or problem(s) studied
Multiple organ failure following traumatic haemorrhage.

Interventions
The trial Intervention arm will be split into two stages:
The first stage will be randomised 2:1 low dose intervention (2.4mg/kg) versus placebo.

The second stage will be randomised 2:1 high dose intervention (4.8mg/kg) versus placebo. As patients will receive all other clinically indicated treatments, there is no risk of ineffective therapy by administration of the trial treatment.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Artesunate

Primary outcome measure
Sequential Organ Failure Score (SOFA) at 48 hours

Secondary outcome measures
1. Maximum Sequential Organ Failure Score (SOFA) over 7 days
2. Total length of hospital stay
3. Total number of days on organ support (as measured by CTCOFR score)
4. Total length of critical care stay
5. Number of ventilator free days
6. Incidence of acute lung injury (as measured by Lung Injury Score)
7. Incidence of acute kidney injury (as measured by RIFLE score)
8. Incidence of infection
9. Mortality (measured at discharge, after 28 days and after 90 days)

Overall study start date
01/04/2015

Completion date
21/09/2019

Eligibility

Key inclusion criteria
1. Adult trauma patients (16 years and above).
2. Activation of the local massive haemorrhage protocol
3. Patients with active, ongoing haemorrhage
4. Agreement for participation is provided on behalf of incapacitated patients by Personal Consultee or Nominated Consultee (i.e. trauma team leader)

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
105

Key exclusion criteria
1. Time of admission more than 2 hours after the time of injury
2. Time of drug administration not attainable within 4 hours of injury
3. Subject not expected to survive more than 48 hours
4. Evidence of severe traumatic brain injury (GCS 3 at scene)
5. Known pregnancy
6. Suspected non-haemorrhagic cause of shock
7. Massive haemorrhage protocol activation more than one hour after arrival
8. Concurrent participation in another Clinical Trial of an IMP
9. Breastfeeding females
10. Known allergy to Artesunate

Date of first enrolment
21/03/2017

Date of final enrolment
21/03/2019

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
The Royal London Hospital
Barts Health NHS Trust
Whitechapel Road
London
United Kingdom
E1 1BB

Sponsor information

Organisation
Queen Mary University of London

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Joint Research & Management Office
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Sponsor type
University/education

ROR
https://ror.org/026zzn846

Funder(s)

Funder type
Charity

Funder Name
Wellcome Trust Grant Number: 101012

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
We intend to present the trial findings in the scientific literature and at medical/scientific conferences. For more wider dissemination, we shall update the Centre's website (http://www.c4ts.qmul.ac.uk/) to share our findings and circulate an article in the Centre's newsletter (http://issuu.com/centrefortraumasciences/docs) that is available from the website and posted out to our public followers via our Twitter feed (@CommsC4TS)

Intention to publish date
31/12/2019

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results			10/05/2021	No	No