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A trial to test tocilizumab, an anti-inflammatory medication, in understanding how controlling the whole body's inflammation can prevent inflammation damage to the brain following head injury

Submission date
09/01/2026

Recruitment status
Recruiting

Registration date
17/03/2026

Overall study status
Ongoing

Last Edited
23/03/2026

Condition category
Injury, Occupational Diseases, Poisoning

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Too much inflammation in the brain is thought to worsen recovery after a head injury, and we think that reducing inflammation might improve patients' outcomes. This study is looking to understand whether treatment with an anti-inflammatory medicine (tocilizumab) might be helpful after a head injury. Tocilizumab is commonly used in other illnesses such as rheumatoid arthritis, and more recently, it has been shown to be effective in treating severe COVID-19. As this is the first study looking at tocilizumab in head injury, it focuses on whether it reduces inflammation in the brain and whether it can be detected in blood samples. If the study is successful, a larger study is planned to investigate definitively whether it improves recovery from head injury.

Who can participate?
Patients at Cambridge University Hospitals NHS Foundation Trust who have suffered a head injury that means they have had to go to intensive care and have a drain in their brain that measures brain inflammation

What does the study involve?
Participants will be involved in two working packages that will run in parallel (with 10 participants recruited into work package 1, and 50 participants recruited into work package 2). If recruited to work package 1, participants will receive either a single dose of tocilizumab or the normal care given to patients with head injury. If recruited to work package 2, participants will randomly (i.e. by chance) be allocated to receive a single dose of either tocilizumab or a saltwater placebo, alongside the usual care given to patients with head injury. For work package 2, the first 14 participants will be recruited to the open-label portion of the work package (where treatment allocation will be known), after which the following 36 participants will be recruited to the double-blind portion of the work package (where participants are randomly

assigned placebo or tocilizumab treatment). In both stages, participants will be followed up for 6 months.

What are the possible benefits and risks of participating?
Current treatment for traumatic brain injury focuses on maintaining the body's normal functions. There is currently no direct treatment for traumatic brain injury. There is no guarantee that a participant will benefit from taking part in this trial, however this trail aims to see whether tocilizumab reduces inflammation in the brain and whether we can detect a beneficial effect via blood samples. Additionally, information collected from participants in this trial may benefit participants with head injuries in the future.

TOCILIZUMAB
As with all medications, tocilizumab has the potential to cause side effects. The most common (occurring in more than 5% of people) side effects include upper respiratory tract infections, nasopharyngitis, headache, hypertension and increased alanine transaminase. As the majority of patients who require intensive care treatment develop nosocomial infections, infection is an expected adverse event for participants in this trial. As an immunosuppressive agent, tocilizumab poses the risk of increasing the severity or duration of an infection and therefore, participants with active, severe infections will be excluded from the trial.

Due to the mechanism of action of tocilizumab, abnormal blood results are an anticipated effect which will be monitored through regular blood tests. Additionally, hypersensitivity to tocilizumab or any of its excipients is an exclusion criterion.
The effects of tocilizumab on pregnancy and the developing foetus are not yet known or fully understood.

BLOOD TESTS
Blood sampling will be via arterial or central venous lines placed as part of standard care during the admission period for participants in the ICU stratum. Participants attending for follow-up will need to undergo a blood draw and may experience the discomfort associated with a needle stick, and may suffer bruising at the site of the needle stick. This will be minimized as much as possible, and only personnel trained in venepuncture will perform this task, and no more than two venepuncture attempts will take place. Whenever possible, blood draws will be combined with those of routine clinical care.

TIME COMMITMENT
There is a substantial time commitment associated with being part of a trial. The number of visits has been minimised as much as possible to help with this.

INCIDENTAL FINDINGS
There is a chance that trial assessments may discover something about the participant's health that they or their Personal Legal Representative are unaware of. In such circumstances, we would discuss the findings with the participant/ Personal Legal Representative as appropriate and inform their GP. If referral to another specialist was required, we would arrange this, in consultation with their GP, if that is what they would like. Such early detection of new medical issues has the benefit of starting treatment early, but, in a small number of cases, may have implications for future employment and insurance.

CONSENT MODEL
Patients will not have the capacity to consent prior to enrolment, with consent being given by the legal representative (personal or professional), which takes place over a short timeframe. Once a patient regains capacity, they will then be approached for their consent, which is after

they have already enrolled and received the trial medication. This, therefore, has the potential to cause distress to the patient. To mitigate this risk, consent activities will be undertaken by appropriate staff members with knowledge and training in this consent model.

All risks are outlined in the consultee and participant information sheet and discussed with the consultee and, where possible, the participant as part of the consent process.

Where is the study run from?
Cambridge University Hospitals NHS Foundation Trust and the University of Cambridge, UK

When is the study starting and how long is it expected to run for?
March 2026 to September 2029

Who is funding the study?
Medical Research Council, UK

Who is the main contact?
cuh.neurosciencecctu@nhs.net

Contact information

Type(s)
Scientific, Public

Contact name
None Study Team

Contact details
CCTU, Box 401. CUH NHS Foundation Trust, Addenbrookes Hospital, Level 6, Coton House, Hills Road
Cambridge
United Kingdom
CB2 0QQ
+44 (0)1223 348498
cuh.neurosciencecctu@nhs.net

Type(s)
Principal investigator

Contact name
None Edward Needham

Contact details
John van Geest Centre for Brain Repair, E D Adrian Building, Forvie Site, Cambridge CB2 0PY
Cambridge
United Kingdom
CB2 0PY
+44 (0)1223 767069
edneedham@doctors.org.uk

Additional identifiers

Integrated Research Application System (IRAS)
1009886

Sponsor's protocol code number
CCTU0447

Study information

Scientific Title
Modulating interleukin-6 pathways to understand the effect of systemic inflammation on detrimental neuroinflammation following traumatic brain injury

Acronym
TITAN-TBI

Study objectives
The main objective of Work Package 1 (WP1) (n = 10) is to assess the pharmacokinetics of tocilizumab in people with traumatic brain injury (TBI).

The main objective of Work Package 2 (WP2) (n = 50) is to assess the impact of tocilizumab treatment on neuroinflammation in people with TBI.

The secondary objectives for WP1 are as follows:
1. To assess the impact of tocilizumab treatment on systemic inflammation in people with TBI
2. To assess the relationships between inflammatory mediators measured in cerebrospinal fluid (CSF) and those measured by cerebral microdialysis (CMD) catheters
3. To establish the feasibility of treating with a monoclonal antibody in the hyperacute phase of TBI within a clinical trial
4. To assess the safety of tocilizumab in people with TBI

The secondary objectives for WP2 are as follows:
1. To assess the impact of tocilizumab treatment on systemic inflammation in people with TBI
2. To evaluate whether tocilizumab reduces biomarkers of brain injury
3. To assess the safety of tocilizumab in people with TBI

Ethics approval required
Ethics approval required

Ethics approval(s)
Submitted 09/01/2026, East of England – Essex REC (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; -; essex.rec@hra.nhs.uk), ref: 26/EE/0024

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Blinded (masking used)

Control
Placebo

Assignment
Parallel

Purpose
Treatment

Study type(s)
Efficacy, Safety, Treatment

Health condition(s) or problem(s) studied
Traumatic brain injury

Interventions
WP1: 10 participants will be recruited to an open-label, non-randomised portion of the trial.
1. Treatment arm: The first 5 participants enrolled into WP1 will receive a single dose of tocilizumab, in addition to standard of care. The dose is based on weight (>40 and ≤65 kg 400 mg, >65 and ≤90 kg 600 mg, >90 kg 800 mg) and will be intravenously administered once at the end of the baseline visit only.
2. WP1 Control arm: After the first 5 participants of WP1 have received tocilizumab, the final 5 participants for WP1 will receive standard of care.

WP2: 50 participants will be recruited to a randomised portion of the trial, where the intervention is determined randomly (i.e., by chance). For the first 14 participants recruited to WP2, treatment will be “open label”, meaning the participant and research team will know what treatment has been allocated. For the remaining participants (participants 15-50), treatment allocation will not be known by the participant or research team (double-blind). Randomisation allocations will be performed by Sealed Envelope.
1. Treatment arm: Participants will receive a single dose of tocilizumab, in addition to standard of care. The dose is based on weight (>40 and ≤65 kg 400 mg, >65 and ≤90 kg 600 mg, >90 kg 800 mg) and will be intravenously administered once at the end of the baseline visit only.
2. WP2 Control arm: Participants will receive a single dose of 100 ml 0.9% saline, in addition to standard of care, which will be intravenously administered once at the end of the baseline visit only.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome(s)

1. WP1 – Penetration of tocilizumab into the central nervous system (CNS) measured using enzyme linked immunosorbent assay (ELISA) to compare peak concentration in CSF against peak blood concentration at drain removal or 24 weeks post-baseline

2. WP2 – Change in inflammatory mediator levels in the CMD measured using Alamar Nulisa proteomic analysis at days 3 and 5 over the first 5 days post-baseline

Key secondary outcome(s)

1. Inflammatory mediator levels in the blood measured using Alamar Nulisa proteomic analysis at days 3, 5 and 7 post-baseline

2. Neurofilament light (NfL) concentrations in the blood measured using Alamar Nulisa proteomic analysis at days 3, 5 and 7, as well as weeks 2 and 6 post-baseline

3. Glial Fibrillary Acidic Protein (GFAP) concentrations in the blood measured using Alamar Nulisa proteomic analysis at days 3, 5 and 7, as well as weeks 2 and 6 post-baseline

4. The number and nature of non-ubiquitous following major head trauma (or ubiquitous if deemed clinically significant) adverse events and serious adverse events measured using data collected from study records at days 3, 5 and 7, as well as weeks 2 and 6 and 24 post-baseline

5. Survival to 28 days, censored at hospital discharge measured using data collected from study records at 24 weeks post-baseline

6. Length of index neurocritical care unit stay, censored measured using data collected from study records at 24 weeks post-baseline

7. Length of index hospital stay, censored measured using data collected from study records at 24 weeks post-baseline

8. Intracranial hypertension therapy intensity level over the first 7 days post-injury measured using data collected from study records at one time point

9. Measures of inflammatory cells and proteins in surplus samples taken for infection surveillance over 24 weeks post-baseline, censored at hospital discharge measured using data collected from study records at one time point

10. Clinical measures of TBI measured using validated functional and cognitive assessment tools (Glasgow Outcome Scale – Extended (GOSE), EuroQol-5 dimensions-5 levels (EQ-5D-5L), Quality of Life after Brain Injury – Overall Scale (QOLIBRI-OS), Patient Health Questionnaire (PHQ-9), Post-traumatic Stress Disorder Checklist for DSM-5 (PCL-5), Rivermead Post Concussion Questionnaire, Generalised Anxiety Disorder Assessment (GAD-7), Sleep Condition Indicator (SCI), Chalder Fatigue Scale (CFS), Post-traumatic epilepsy questionnaire, Galveston Orientation and Amnesia Test (GOAT), Rey Auditory Verbal Learning Test (RAVLT), Trail Making Test (TMT) Parts A & B, National Adult Reading Test (NART) and Brief Pain Inventory – Short Form (BPISF)) at 24 weeks post-injury

Completion date

30/09/2029

Eligibility

Key inclusion criteria
The main inclusion criteria for both WPs are as follows:
1. Have had Legal Representative consent given
2. Be aged 18 years or older
3. Have moderate to severe post-resuscitation TBI (Glasgow Coma Scale (GCS) <13)

Additional inclusion criteria for WP1 are:
1. Have an external ventricular drain (EVD) and a catheter sited for clinical care

Additional inclusion criteria for WP2 are:
1. Have a CMD catheter in situ (or plan to site within the requisite timeframe for investigational medicinal product administration i.e. 48 hours post-injury)

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
110 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
Current exclusion criteria as of 23/03/2026:
The main exclusion criteria for both WPs are as follows:
1. Brain injury or comorbidity deemed incompatible with survival
2. Timing of injury such that it is clear IMP/placebo could not be delivered within 48 hours (e.g., delayed secondary transfer from peripheral hospital; WP2 only)
3. Known allergy to tocilizumab or any of its excipients
4. Contraindications of the IMP as listed in the Summary of Product Characteristics (SmPC)
5. Weight <50 kg
6. Active severe infection
7. Perforated viscus on cross-sectional imaging
8. Neutropoenia <1 x 10^9/litre at screening
9. Alanine aminotransferase (ALT) > 5x upper limit of normal at screening
10. Thrombocytopoenia <50 x 10^3 / microlitre at screening
11. Actively taking immunosuppression medications (e.g. immunotherapy) or known immunodeficiency disorder (n.b. adequately treated HIV ≠ exclusion criterion)
12. Pregnant or breastfeeding
13. Received tocilizumab within 30 days prior to the screening visits
14. Prior receipt of any other investigational medicinal product, or participation in another interventional clinical trial, within 30 days or 5 half-lives after the last IMP dose (whichever is

longer) before the first dose of study treatment
15. Use of medication metabolised by CYP450 3A4, 1A2 or 2C9 which, in the opinion of the investigator, will put the participant at risk if the drug level would significantly decrease for a period of time following a single dose of tocilizumab
16. Any other significant disease, disability or investigation result which, in the opinion of the Investigator, may either put the participant at risk, or may influence the result of the trial, or the participant's ability to participate in the trial

Previous exclusion criteria:
The main exclusion criteria for both WPs are as follows:
1. Brain injury or comorbidity deemed incompatible with survival
2. Timing of injury such that it is clear IMP/placebo could not be delivered within 48 hours (e.g., delayed secondary transfer from peripheral hospital; WP2 Only)
3. Known allergy to tocilizumab or any of its excipients
4. Weight ≤40 kg
5. Contraindications of the IMP as listed in the Summary of Product Characteristics (SmPC)
6. Active severe infection
7. Perforated viscus on cross-sectional imaging
8. Neutropoenia <1 x 10^9/litre at screening
9. Alanine aminotransferase (ALT) > 10x upper limit of normal at screening
10. Thrombocytopoenia <50 x 10^3 / microlitre at screening
11. Actively taking immunosuppression medications (e.g. immunotherapy) or known immunodeficiency disorder (N.B. adequately treated HIV ≠ exclusion criterion)
12. Pregnant or breastfeeding
13. Received tocilizumab or any other investigational drug within 30 days prior to the screening visit
14. Use of medication metabolised by CYP450 3A4, 1A2 or 2C9 which, in the opinion of the investigator, will put the participant at risk if the drug level would significantly decrease for a period of time following a single dose of tocilizumab
15. Any other significant disease, disability or investigation result which, in the opinion of the Investigator, may either put the participant at risk, or may influence the result of the trial, or the participant's ability to participate in the trial

Date of first enrolment
01/03/2026

Date of final enrolment
31/12/2028

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Addenbrookes Hospital
Hills Road

Cambridge
England
CB2 0QQ

Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust

ROR
https://ror.org/04v54gj93

Organisation
University of Cambridge

ROR
https://ror.org/013meh722

Funder(s)

Funder type

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be stored in a non-publicly available repository

IPD sharing plan summary

Stored in non-publicly available repository