ISRCTN28447330 https://doi.org/10.1186/ISRCTN28447330

WHiTE13-DECI: An investigation of people 60 years and over with a broken hip to determine whether they are less likely to have delirium after hip surgery if we treat them with infliximab during the operation

Submission date 02/11/2023	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 20/02/2024	**Overall study status** Ongoing	
Last Edited 25/09/2025	**Condition category** Musculoskeletal Diseases	

Plain English summary of protocol

Background and study aims

This study has been designed following a James Lind Alliance Patient and Public Research Priority Setting Partnership, which identified the following question as a key research priority: “What are the best treatments to prevent and treat confusion and delirium after surgery in adults with a broken bone in the leg?” The study has been co-produced with the UK Musculoskeletal Trauma Patient and Public Involvement Group. A broken hip (hip fracture) is a very serious injury that requires surgery to repair or replace the broken bone followed by a long period in hospital to recover. Around a quarter of patients with hip fractures die within a year and those that survive have a permanent loss of quality of life. Worldwide there are 1.3 million hip fractures each year, with more than 70,000 in the UK. Around a quarter of patients who have a hip fracture have an episode of ‘delirium’ around the time of their surgery. Delirium is a condition where the patient loses awareness of themselves and their environment, and has difficulty thinking clearly. For relatives and friends, and the patient, delirium is very disturbing. The symptoms of delirium are similar to those of patients with dementia but develop over a short period and tend to vary over time. In the short-term, delirium leads to longer stays in hospital and an increased risk of complications including death. In the longer term, delirium is closely linked with an increased risk of developing dementia. Delirium is thought to be caused by inflammation in the brain. The inflammation is triggered by the injury and is thought to get worse during surgery. This study will investigate a drug called infliximab which is given during surgery. Infliximab is a powerful anti-inflammatory drug. This study aims to decide if patients who have operations on broken hips are less likely to have delirium if we treat them with infliximab during the operation.

Who can participate?

Patients aged over 60 years with a hip fracture, apart from the very small number of patients who do not have an operation on their hip.

What does this study involve?
Patients at approximately 8 hospitals in the UK will be approached to take part in the study. 416 participants will take part, with half being allocated by chance to receiving infliximab, and half to receiving a placebo containing no infliximab. Neither the patients nor their doctors will know which treatment they had to make the study fair. All other elements of the patient's treatment will follow the normal care pathway for all hip fracture patients at the hospital. Baseline information including pre-injury mobility and residential status will be collected. Participants or their proxies will also be asked to complete the EQ-5D-5L questionnaire to indicate their typical pre-injury quality of life status. A simple questionnaire called the Memorial Delirium Assessment Scale (MDAS) will be used to measure symptoms of delirium in the first five days after surgery. Participants' mobility, quality of life and complications, including the risk of infection and developing dementia in the 12 months after surgery will also be measured. Some of the study participants may be asked to consent to have their brain waves monitored during surgery and to have small blood samples taken before and in the days after surgery to measure the level of inflammation in the blood.

What are the possible benefits and risks of participating?
Infliximab is already used very widely in the NHS as a treatment for a range of diseases, but it has not been tested to see if it could help prevent delirium after surgery.
Hip fracture surgery carries some risk, including infection in the surgical wound, blood clots, chest or urine infection. These risks are the same for people who are not part of this research project.
There is a small risk of undesirable reactions to the injection of infliximab such as headache, nausea and throat or sinus infections. Very rarely, some people can develop an allergic reaction to infliximab. Patients will have continuous monitoring whilst the infliximab is being given, so if this were to happen during surgery, the anaesthetist would treat the reaction as per normal clinical care.
There is a very small risk that the infliximab may cause old infections of tuberculosis and hepatitis to come back again. Long-term repeated use of infliximab affects the immune system so can make you more likely to develop infections but in this case, as it will only be administered once, it is very unlikely that this will occur.

Where is the study run from?
University of Oxford (UK)

When is the study starting and how long is it expected to run for?
November 2022 to February 2027

Who is funding the study?
National Institute for Health and Care Research (NIHR) (Grant Code: NIHR203127)

Who is the main contact?
Central trial team, white13-deci@ndorms.ox.ac.uk

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
2020-003719-83

Integrated Research Application System (IRAS)
287755

Central Portfolio Management System (CPMS)
58857

Study information

Scientific Title
A feasibility study for a randomised controlled comparison on the effect of infusion of anti-TNF or placebo during surgery on delirium symptoms between hip fracture patients over 60 years of age

Acronym
WHiTE13-DECI

Study objectives
To investigate if an infusion of the anti-TNF agent infliximab during surgery has an effect on delirium symptoms in the immediate post-operative period and on the development of cognitive impairment, quality of life and mortality in the following year.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 14/01/2021, South Central - Berkshire Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8178; berkshire.rec@hra.nhs.uk), ref: 20/SC/0452

Study design
Multicentre two-arm randomized placebo-controlled superiority comparison with embedded exploratory mechanistic outcome study

Primary study design

Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Hip fracture

Interventions
WHiTE 13 DECI is a randomised comparison appended to the World Hip Trauma Evaluation (WHiTE) Platform. WHiTE is a platform trial designed to efficiently deliver multiple randomised comparisons of interventions for patients aged 60 years and over with a hip fracture. The Platform and its appended randomised comparisons are governed by one single set of ethical and regulatory approvals and an explicit legal basis and processing purpose for the use of patient-level data. The Platform affords a common core dataset and documentation.

Individual randomised comparisons are not dependent on each other and each will have unique start and stop dates and publication of results without compromising the integrity of the Platform.

Specifically for WHiTE 13-DECI: Participants will be allocated on a 1:1 basis to either placebo or infliximab infusion treatments.
• Intervention: Single infusion of infliximab at 5mg/kg body weight, diluted in 250ml of 0.9% saline and administered intravenously over 2 hours
• Placebo control: Identical volumes of 0.9% saline

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome(s)
Peak postoperative delirium measured using the Memorial Delirium Assessment Scale (MDAS) on days 1-5 after surgery

Key secondary outcome(s))
1. Cognitive impairment measured using the Telephone Interview for Cognitive Status (TICS) at 4 and 12 months post-diagnosis of a hip fracture
2. Health-related quality of life measured using the Euroqol-5D-5L pre-injury, at 4 and 12 months post-diagnosis of a hip fracture
3. Mortality risk measured using death notification up to 12 months post-diagnosis of a hip fracture
4. Subjective mobility status measured using the UK National Hip Fracture Database Mobility Scale at 4 and 12 months post-diagnosis of a hip fracture
5. Residential status measured using the UK National Hip Fracture Database Residential Status

at 4 and 12 months post-diagnosis of a hip fracture
6. Risk and pattern of complications measured using bespoke reporting forms up to 12 months post-diagnosis of a hip fracture

Completion date
28/02/2027

Eligibility

Key inclusion criteria
Adults aged 60 years or over diagnosed with a hip fracture that in the opinion of the treating surgeon may benefit from surgical treatment

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
60 years

Sex
All

Key exclusion criteria
Current exclusion criteria as of 25/09/2025:
1. The patient has severely impaired renal function eGFR <30 ml.min-1
2. The patient has severely impaired hepatic function
3. The patient is currently taking any anti-TNF drug
4. The patient has a contra-indication to anti-TNF injection
5. The patient has a known hypersensitivity to any anti-TNF agent or any of the excipients
6. The patient has known active tuberculosis (TB) or a history of TB or is at risk of developing TB e.g. through the use of immunosuppressants
7. The patient has another known active infection (chronic or localised) or known history of recurring infections or conditions which may predispose patients to infection, including the use of concomitant immunosuppressive medications
8. The patient has known lung fibrosis
9. The patient had systemic inflammatory disorder such as rheumatoid arthritis or inflammatory bowel disease
10. The patient has known moderate to severe heart failure (NYHA class III/IV)
11. The patient has HIV, Hepatitis B or C (based on medical history)
12. The patient is at risk of Hepatitis B or HIV infections, including intravenous drug use
13. The patient has been diagnosed with Multiple Sclerosis (MS) or other central or peripheral nervous system demyelinating disorders
14. History of malignancy within 5 years prior to screening or any evidence of persistent malignancy, except basal cell or squamous cell carcinomas of the skin, or cervical carcinoma in

situ which has been treated or excised in a curative procedure
15. The patient has had a live vaccination 4 weeks prior to study entry or will require one within 12 weeks after the study intervention
16. The patient takes biologics including anakinra or abatacept or DMARDS.
17. The patient is or has been a participant in a clinical trial of a medicinal product in the last 12 weeks

Previous exclusion criteria:
1. The patient has severely impaired renal function eGFR <30 ml.min-1
2. The patient has severely impaired hepatic function
3. The patient is currently taking any anti-TNF drug
4. The patient has a contra-indication to anti-TNF injection
5. The patient has a known hypersensitivity to any anti-TNF agent or any of the excipients
6. The patient has known active tuberculosis (TB) or a history of TB or is at risk of developing TB e.g. through the use of immunosuppressants
7. The patient has another known active infection (chronic or localised) or known history of recurring infections or conditions which may predispose patients to infection, including the use of concomitant immunosuppressive medications
8. The patient has known lung fibrosis
9. The patient had systemic inflammatory disorder such as rheumatoid arthritis or inflammatory bowel disease
10. The patient has known moderate to severe heart failure (NYHA class III/IV)
11. The patient has HIV, Hepatitis B or C (based on medical history)
12. The patient is at risk of Hepatitis B or HIV infections, including intravenous drug use
13. The patient has been diagnosed with Multiple Sclerosis (MS) or other central or peripheral nervous system demyelinating disorders
14. The patient has ever been diagnosed with cancer or current suspected cancer, except basal cell carcinoma (BCC/rodent ulcer)
15. The patient has had a live vaccination 4 weeks prior to study entry or will require one within 12 weeks after the study intervention
16. The patient takes biologics including anakinra or abatacept or DMARDS.
17. The patient is or has been a participant in a clinical trial of a medicinal product in the last 12 weeks

Date of first enrolment
15/03/2024

Date of final enrolment
30/09/2025

Locations

Countries of recruitment
United Kingdom

Study participating centre
-
United Kingdom
-

Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

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 are/will be available upon request from the Lead Investigator (Prof. Matt Costa, matthew.costa@ndorms.ox.ac.uk). Each request will be reviewed and decided upon on a case-by-case basis. Participants will be informed via the Participant Information Sheet (and will consent to the contents of this PIS) of the possibility of de-identified datasets being made available following appropriate requests.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file		25/09/2025	25/09/2025	No	No