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A trial to test the use of deferiprone in people with neuroferritinopathy

Submission date
21/04/2023

Recruitment status
Recruiting

Registration date
02/04/2024

Overall study status
Ongoing

Last Edited
22/08/2024

Condition category
Nervous System Diseases

[X] 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
Neuroferritinopathy is a disorder caused by a mutation (fault) in a gene which leads to iron gradually building up in the brain. The build-up of iron eventually leads to the death of brain cells (called neurons), and certain brain regions that help control movement are particularly affected.

There are no treatments known to reduce or slow the progression of neuroferritinopathy. Some treatments are available to help with the symptoms of neuroferritinopathy, but these may only be effective for a limited amount of time and have significant side effects.

Deferiprone is a medication that is used to remove excess iron from the body and is licensed for use in the UK for a condition called thalassaemia major. It has been shown in a related disorder that deferiprone is able to reduce brain iron and slow clinical progression, and we now want to test this in people with neuroferritinopathy. The purpose of the trial is to test whether deferiprone can reduce the iron build-up in the brain of people with neuroferritinopathy.

Who can participate?
To be eligible, participants must have a genetic diagnosis of neuroferritinopathy, be aged 16 or over, and fulfil additional eligibility criteria.

What does the study involve?
Participants in this trial will take tablets twice a day for 12 months. There is a 50% chance (much like flipping a coin) that the tablets will contain deferiprone. The other half of participants will receive a ‘dummy drug’ called a placebo. Neither the participant nor the trial doctor will know which treatment is being taken, although the trial doctor can find out if necessary.

The trial is being conducted in Cambridge, although participants may be recruited from elsewhere. Participants will need to attend four in-person visits in Cambridge over a 12-month period, as well as have monthly phone calls and regular blood tests between the in-person visits. A final phone visit will take place at 13 months.

What are the possible benefits and risks of participating?
Benefits:
Not provided at time of registration
Risks:
Potential risks, and the voluntary nature of taking part in research, are fully detailed in the participant information sheet.

DEFERIPRONE
Like any medication, deferiprone has potential side effects. The most common (more than 10%) side effects include nausea, abdominal pain, neutropenia, vomiting and abnormal colouring of the urine. Due to the mechanism of action of deferiprone (and in line with the effects observed in a study in a related indication), anaemia is an anticipated effect. We will monitor for this via regular blood tests. Contraindication to deferiprone is an exclusion criterion.

Participants will be required to use two highly efficient forms of contraception for the duration of treatment and for a minimum of 1 sperm cycle (defined as 90 days)/menstruation cycle (defined as 30 days) after the end of treatment due to possible teratogenic effects of deferiprone. Additionally, for participants of childbearing potential, regular pregnancy tests will be performed.

Participants will be provided with a large quantity of IMP which means there is greater potential for IMP to be taken incorrectly. To mitigate this, participants will be asked to detail the number of unopened full bottles of medication as part of the monthly phone calls, alongside a verbal review of the medication diary. If there are clinical concerns for an individual participant (e.g. there is evidence of overdosing) then the CI will review on a case-by-case basis and determine appropriate actions (e.g. dispensing on a more regular basis, so the amount of IMP a participant has at any one time is reduced). Any mitigating actions will be at the CI's discretion.

BLOOD TESTS
Blood tests can cause minor discomfort and bruising of the skin. Standard protocols will be followed to prevent infections.

Due to the use of deferiprone, regular blood testing is required to monitor for any safety concerns. In order to reduce the burden of these regular blood tests, we have appointed a third party who will go to a location (such as home or workplace) which will be suitable for the participant to take the blood samples.

MRI SCANS
Although MRI scanning is generally very safe, there are certain circumstances where it must be avoided. We will go through a checklist to check it is safe for the participants to undergo the scans and potential participants will be excluded if there are any contraindications to them having MRI scans.

Participants will be required to lie as still as possible in a small and enclosed space in the MRI machine for up to 1 hour, which they may find claustrophobic. During scans, the participants will be in constant contact with the trial team and can ask to stop the scan at any point.

There is a chance (less than 1:100) that the MRI scan shows a significant abnormality that the participant was not aware of. In such circumstances, the participant would be counselled and will be referred to an appropriate specialist in consultation with their GP if they are agreeable. Such early detection has the benefit of starting treatment early but, in a small number of cases, may have implications for future employment and insurance.

TIME COMMITMENT
There is a substantial time commitment associated with being part of a trial. Face-to-face visits have been reduced to a minimum, whilst retaining safety checks, in order to reduce the burden on participants.

PARTICIPATION IN OTHER TRIALS
Participants will not be able to participate in any other CTIMPs whilst participating in this trial.

Where is the study run from?
Cambridge Clinical Trials Unit (UK)

When is the study starting and how long is it expected to run for?
April 2023 to February 2026

Who is funding the study?
LifeArc (UK)

Who is the main contact?
Prof Patrick Chinnery, pfc25@medschl.cam.ac.uk
Kerry Dresser, kld57@cam.ac.uk

Contact information

Type(s)
Principal Investigator

Contact name
Prof Patrick Chinnery

Contact details
Neurology Unit Level 5 ‘A’ Block
Box 165
Addenbrooke’s Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ
-
pfc25@medschl.cam.ac.uk

Type(s)
Scientific

Contact name
Ms Kerry Dresser

Contact details
Department of Clinical Neurosciences
Cambridge Clinical Trials Unit
Addenbrooke's Hospital

Hills Road
Cambridge
United Kingdom
CB2 0QQ
-
kld57@cam.ac.uk

Additional identifiers

EudraCT/CTIS number
2022-000216-58

IRAS number
1006406

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CCTU0335, IRAS 1006406, CPMS 58605

Study information

Scientific Title
A randomised, double-blind, placebo-controlled trial examining the safety and efficacy of deferiprone in patients with neuroferritinopathy

Acronym
DefINe

Study objectives
Primary objective:
To determine whether deferiprone reduces brain iron levels compared to placebo in individuals affected by neuroferritinopathy.

Secondary objectives:
1. To assess the safety and tolerability of deferiprone in people with neuroferritinopathy
2. To assess the effect of deferiprone on MRI parameters in people with neuroferritinopathy
3. To assess the effect of deferiprone on clinical outcome measures of dystonia and chorea, and quality of life

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval pending, ref: 23/WA/0145

Study design
Interventional double blind randomized parallel group placebo controlled trial

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Neuroferritinopathy

Interventions
DefINe is a randomised, double-blind, placebo-controlled trial which aims to test the use of deferiprone in people with neuroferritinopathy. We are aiming to recruit 40 participants overall. Participants will attend 4 visits (Screening, Day 0, Month 6 and Month 12) for trial assessments, interim trial assessments will be conducted at home/via phone. Study participants will be randomised 1:1 to either Deferiprone (30 mg/kg/day - administered orally) or Placebo group. Total trial duration for each participant will be 14 months, consisting of a 4 week screening period and a 12 month treatment period. The end of trial visit will be performed at month 13.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome measure
Change in the mean T2* relaxation rate in the thalamus measured by 7T MRI between baseline and month 12.

Secondary outcome measures
1. The number of AEs or withdrawals that are attributable to deferiprone from baseline (day 0) to end of trial visit (month 13)
2. The change in the mean T2* relaxation rate in the thalamus measured by 7T MRI between baseline and month 6
3. The regional brain structural change, measured using voxel-based morphometry, between baseline and month 12
4. The change in dystonia and chorea rating scales (using BADS, UDRS, and UHDRS) between baseline and month 12
5. The change in quality of life measures (using SF-36) between baseline and month 12

Overall study start date

19/04/2023

Completion date
01/02/2026

Eligibility

Key inclusion criteria
1. Be aged 16 years and over, of any sex and gender
2. Be willing and able to provide written informed consent
3. Have a genetic diagnosis of neuroferritinopathy (mutations in FTL gene)
4. Have symptomatic neuroferritinopathy
5. Be able to undergo MRI brain imaging
6. Agree to use contraception if required
7. Be able (in the Investigator's opinion) and willing to comply with all trial requirements

Participant type(s)
Patient

Age group
Adult

Lower age limit
16 Years

Sex
Both

Target number of participants
40

Key exclusion criteria
1. Conditions or use of medicines known to contraindicate the use of deferiprone (e.g. history of agranulocytosis or recurrent episodes of neutropenia) or known hypersensitivity to deferiprone or any of its excipients
2. Neutropenia (absolute neutrophil count [ANC] < 1.0 x 10^9/L) at the screening visit
3. Unable or unwilling to undergo the required blood testing
4. Inability to take or swallow oral medication
5. Pregnant, breastfeeding or planning to become pregnant during the trial
6. Received an investigational drug (including investigational vaccines) or used an invasive investigational medical device within 30 days before the screening assessment, or currently enrolled in an interventional investigational trial
7. Currently taking any other iron chelator(s), or taken any other iron chelator(s) within three weeks of the screening visit
8. Currently taking medicines that are known to cause agranulocytosis or are associated with neutropenia
9. Previous treatment with deferiprone with a serious adverse reaction (SAR) requiring withdrawal of deferiprone
10. Patients who, in the opinion of the Investigator, represent a high medical or psychological risk

11. Active drug or alcohol use or dependence that, in the opinion of the Investigator, would interfere with adherence to trial requirements
12. Movement disorder preventing brain imaging
13. Any other condition which, in the opinion of the Investigator, makes the patient inappropriate for entry into the trial

Date of first enrolment
05/06/2024

Date of final enrolment
01/02/2026

Locations

Countries of recruitment
United Kingdom

Study participating centre
Cambridge University Hospitals NHS Foundation Trust
Addenbrookes Hospital
Cambridge
United Kingdom
CB2 0AU

Sponsor information

Organisation
Cambridge Clinical Trials Unit

Sponsor details
Regulatory Team
Room 200, Bay 13
Clifford Allbutt Building
Biomedical Campus
Hills Road
Cambridge
England
United Kingdom
CB2 0QQ
+44 1223 349760
cuh.ccturegulatory@nhs.net

Sponsor type
University/education

Funder(s)

Funder type
Industry

Funder Name
LifeArc

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Peer reviewed scientific journals
Conference presentation
Publication on website
Other publication
Submission to regulatory authorities

Intention to publish date
30/11/2026

Individual participant data (IPD) sharing plan
No identifiable data will be shared. Fully de-identified data may be provided, for the purpose of health and care research, to researchers running other research studies in Cambridge and in other organisations which may be universities, NHS organisations or companies involved in health and care research in the UK or abroad. This is fully detailed within the participant information sheet and informed consent form.

IPD sharing plan summary
Data sharing statement to be made available at a later date