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A trial to look at how different doses of felodipine are tolerated in people with early-stage Huntington's disease

Submission date
05/05/2022

Recruitment status
No longer recruiting

Registration date
08/07/2022

Overall study status
Completed

Last Edited
28/05/2025

Condition category
Nervous System Diseases

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

Plain English summary of protocol

Background and study aims
Huntington's disease (HD) is an inherited condition that causes damage to cells in the brain over time due to the production of an abnormal protein called mutant huntingtin (mHTT). Currently, there is no cure for HD and its progress cannot be reversed or slowed down.
One way to try and stop HD from progressing is to increase (upregulate) its clearance from cells. One normal process that cells use to clear proteins (including mHTT) is called autophagy.

Felodipine is a drug which has been shown in animal models to upregulate the autophagy process. The purpose of this trial is to test the safety and tolerability of different doses of felodipine in early-stage HD.

Who can participate?
18 participants will be recruited, aged 35-70 years (inclusive) with genetically and clinically confirmed early-stage HD.

What does the study involve?
Participants will be assigned to one of three dosing cohorts (6 participants per cohort) in an alternating fashion, where participant 1 will be allocated to cohort 1, participant 2 will be allocated to cohort 2, participant 3 will be allocated to cohort 3, participant 4 will be allocated to cohort 1, and so on:
- Cohort 1: start on 2.5mg, increase to 5mg at week 2 and stay on 5mg until week 58
- Cohort 2: start on 2.5mg, increase to 5mg at week 2, increase to 10mg at week 4, and stay on 10mg until week 58
- Cohort 3: start on 2.5mg, increase to 5mg at week 2, increase to 10mg at week 4, increase to 20mg at week 6, and stay on 20mg until week 58
The dose will only be increased if it has been tolerated at the previous lower dose. If a dose is not tolerated, the participant will be reduced back to the previous dose that was tolerated.
The trial duration will be up to 66 weeks, including a 4-week screening window, 58-week treatment period, and a 4-week wash out period, concluding with an end of trial visit at week 62.

What are the possible benefits and risks of participating?
Benefits:
There is no guarantee that participants will benefit from taking part in this trial. Participants may experience relief in their symptoms or a slowing of their disease progression. However, information collected as part of this trial may benefit people with HD in the future.
Risks:
As felodipine is licensed to treat high blood pressure, a reduction in blood pressure or low blood pressure are anticipated effects of the IMP. All participants will be closely monitored for these effects, which will include participants taking at-home blood pressure readings and reporting these to the trial team. Doses that are not tolerated will be reduced.

In addition, according to the Neofel XL 2.5mg prolonged release tablets (Fannin UK/Kent Pharma UK Ltd.) SmPC (chosen as the reference safety information for this trial), the most common side effects of felodipine include: ankle swelling, headache and flush. Felodipine side effects are mostly dose dependent and usually appear at the start of treatment or after dose increase. These side effects are usually short lived and decrease over time. All participants will be closely monitored for side effects. Doses that are not tolerated will be reduced. Contraindication to felodipine is a reason for somebody not being included in the trial.

There is a risk of overdose if the participants take too many tablets. Participants will receive clear instruction on dosing by the trial team, both verbally and within the medication diary, to minimise this risk.

Blood collection can cause minor discomfort and bruising. Standard protocols will be followed to prevent infection and reduce risk.

MRI scans may (1:100 chance) show a significant abnormality that the participant was unaware of. In such cases, participants will be counselled and referred as appropriate. Such detection has the benefit of starting early treatment but may have implications for employment and insurance. The MRI scanner tunnel is narrow and may cause anxiety and claustrophobia. During scans, the participant will be in constant contact with the trial team and can stop the scan at any point. MRIs in this trial are optional.

Some trial assessments involve sensitive topics such as depression and suicide, which may be uncomfortable for participants to discuss. These will only be performed by trained team members who will discuss any issues that arise with the participant. Following consultation, the participant may be referred as appropriate.

Felodipine is not recommended during pregnancy. Women of childbearing potential are required to use one highly effective method of contraception for the duration of the trial. Participants who become pregnant whilst on the trial may be withdrawn. Permission to follow any pregnancy will be requested.

Trial participation will involve a substantial time commitment. This, and the voluntary nature of participation, will be fully detailed in the PIS.

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?
May 2022 to April 2024

Who is funding the study?
1. UK Dementia Research Institute
2. National Institute for Health Research (NIHR) Cambridge Biomedical Research Centre (BRC) – Dementia and Neurodegeneration Theme (UK)

Who is the main contact?
Dr Roger Barker, rab46@cam.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Study Team

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Additional identifiers

EudraCT/CTIS number

2021-000897-27

IRAS number
1004614

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CCTU0265, IRAS 1004614

Study information

Scientific Title
FELL-HD: A trial to assess the tolerability of using felodipine to upregulate autophagy as a treatment of Huntington's disease

Acronym
FELL-HD

Study objectives
To test the safety and tolerability of different doses of felodipine in early-stage HD.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 16/07/2022, London - Brent REC (Health Research Authority, Skipton House, 80 London Road, London, SE1 6LH, UK; +44 20 7104 8137; brent.rec@hra.nhs.uk), ref: 22/LO/0387

Study design
Interventional non randomized

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Huntington disease

Interventions
Cohort 1: Doses given at 2.5 mg to 5 mg once daily for 58 weeks (2.5 mg for two weeks, followed by 5 mg until week 58). Oral administration.
Cohort 2: Doses given at 2.5 mg to 10 mg once daily for 58 weeks (2.5 mg for two weeks, 5 mg for two weeks, followed by 10 mg until week 58). Oral administration.
Cohort 3: Doses given at 2.5 mg to 20 mg once daily for 58 weeks (2.5 mg for two weeks, 5 mg for two weeks, 10 mg for two weeks, followed by 20 mg until week 58). Oral administration.

For any of the dosing cohorts, if a dose is not tolerated then the participants' felodipine will be reduced down to the last dose which was tolerated.

Participants will be followed up for an additional 4 weeks after stopping felodipine (i.e. to week 62 for all cohorts).

Intervention Type
Drug

Phase
Phase II

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

Primary outcome measure
The number of adverse events attributable to felodipine from baseline (week 0) to final visit measured using participant records and participant-reported events

Secondary outcome measures
There are no secondary outcome measures

Overall study start date
03/05/2022

Completion date
30/04/2024

Eligibility

Key inclusion criteria
1. Have given written informed consent
2. Be male or female, aged 35 to 70 years (inclusive)
3. Be a fluent English speaker, as assessed by the trial team during the screening visit, to enable completion of the cognitive assessments
4. Have early disease, as defined by a Unified Huntington's disease Rating Scale (UHDRS) total functional capacity (TFC) score ≥9
5. Have a diagnostic confidence level (DCL) of ≥2

Participant type(s)
Patient

Age group
Adult

Lower age limit
35 Years

Upper age limit
70 Years

Sex
Both

Target number of participants
18

Total final enrolment
18

Key exclusion criteria
1. Participant has dementia (as defined by MMSE <24 and/or ACE-III <82) or lacks capacity to consent for themselves
2. Significant co-morbidities which, in the opinion of the Principal Investigator (PI), precludes inclusion in the trial
3. Ongoing medical or psychiatric condition that is not, in the opinion of the PI, adequately managed
4. Vital sign abnormality which, in the opinion of the PI, precludes inclusion in the trial including symptomatic hypotension
5. Poorly controlled features of HD, as indicated by a change in HD medication within 3 months of screening
6. Contraindications to felodipine, including taking any medication known to significantly interact with felodipine
7. Participant is currently taking a calcium channel blocking anti-hypertensive medication or has taken a calcium channel blocking anti-hypertensive medication within 12 weeks of the screening visit'
8. Known allergy to felodipine, any other dihydropyridine (due to theoretical risk of cross-hypersensitivity), or excipients of felodipine tablets
9. Presence of rare hereditary problem of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption as the felodipine tablets contain lactose
10. Participant is currently taking felodipine or has taken felodipine within 12 weeks of the screening visit
11. Female participant of childbearing potential who is unwilling or unable to use one highly effective method of contraception during the trial, as felodipine is not recommended to be taken during pregnancy (as per the BNF)
12. For the purpose of the trial, a woman is considered to be of childbearing potential following menarche until postmenopausal, unless surgically sterile. Permanent sterilisation methods include hysterectomy, bilateral salpingectomy, and bilateral oophorectomy. A postmenopausal state is defined as no menses for 12 months without an alternative medical cause.
13. Female participant who is pregnant or breastfeeding
14. Participant has received an investigational drug (including investigational vaccines) or used an invasive investigational medical device within 4 weeks prior to the screening visit, or was enrolled in an interventional investigational trial within 4 weeks prior to screening

15. Any other significant disease, disability or investigation result which, in the opinion of the PI, 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
17/08/2022

Date of final enrolment
03/01/2023

Locations

Countries of recruitment
United Kingdom

Study participating centre
John van Geest Centre for Brain Repair
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Sponsor information

Organisation
Cambridge Clinical Trials Unit

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Sponsor type
Hospital/treatment centre

Funder(s)

Funder type
Research organisation

Funder Name
UK Dementia Research Institute

Alternative Name(s)
UK DRI Ltd, UK DRI

Funding Body Type
Private sector organisation

Funding Body Subtype
Research institutes and centers

Location
United Kingdom

Funder Name
NIHR Cambridge Biomedical Research Centre

Alternative Name(s)
Cambridge Biomedical Research Centre, NIHR Cambridge BRC, National Institute for Health Research Cambridge Biomedical Research Centre

Funding Body Type
Government organisation

Funding Body Subtype
Local government

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
Other

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. Sharing of de-identified data with collaborators will be an optional part of the consent form.

Intention to publish date
01/03/2025

Individual participant data (IPD) sharing plan
Fully de-identified data will be passed to the public domain (i.e. on an open access data repository/journal) once sufficient validation has been conducted, and meaningful analysis and publication is complete.

IPD sharing plan summary
Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 2.0	09/06/2022	09/08/2022	No	Yes
HRA research summary			26/07/2023	No	No
Protocol article		21/08/2024	23/08/2024	Yes	No
Basic results		28/05/2025	28/05/2025	No	No
Statistical Analysis Plan			28/05/2025	No	No