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DAPA-PD: a trial to test the use of dapansutrile, an anti-inflammatory medication, in people with Parkinson's disease

Submission date
11/01/2025

Recruitment status
Recruiting

Registration date
11/03/2025

Overall study status
Ongoing

Last Edited
09/05/2025

Condition category
Nervous System Diseases

[ ] 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
In Parkinson's disease, an area of the brain called the substantia nigra, loses nerve cells (called neurons) which produce a chemical called dopamine. Dopamine plays a vital role in regulating the movement of the body, and a reduction of dopamine is responsible for many of the symptoms of Parkinson's disease. Research has suggested that inflammation in the brain may contribute to this loss of nerve cells.
We want to find out whether using a medication called dapansutrile can reduce inflammation in the brain in people with Parkinson's, and whether it has an impact on the progression of Parkinson's disease.
Dapansutrile is a medication which acts by suppressing inflammation. Dapansutrile is not yet licensed, which means it is not approved for use in any disease area or in any country. However, it has been used in clinical trials, including in people with heart failure, acute gout, COVID-19, and melanoma. In these trials, dapansutrile has been shown to be safe for use in people.

Who can participate?
Patients aged 50 to 80 years (inclusive) with early Parkinson's disease

What does the study involve?
There are two main parts of the study:
1. Randomised, placebo-controlled phase: where two-thirds of the participants will receive dapansutrile and a third will receive a 'dummy drug' called a placebo for 26 weeks. Neither the participant nor the trial doctor will know which treatment is being taken, although the trial doctor can find out if necessary.
2. Optional open-label phase: where all participants who agree to take part in this section will receive dapansutrile for an additional 26 weeks (whether or not they have received dapansutrile in the first part).
The trial is being conducted in Cambridge. Participants will need to attend 10 in-person visits during the randomised, placebo-controlled phase. If the participant does not wish to continue to the optional open-label phase, they will attend one final in-person visit. If they do agree to take part in the open-label phase, they will attend an additional 7 visits during the open-label phase.

What are the possible benefits and risks of participating?
There is no guarantee that there will be any direct benefits for the participants. Based on previous research, the researchers believe that anti-inflammatory medications might have benefits in early Parkinson's. It is possible that participants may experience relief in their Parkinson's symptoms or an improvement in their disease, but the effects of the trial medication are currently unknown. Taking part in the study will contribute to medical knowledge and information collected as part of the trial may significantly benefit people with Parkinson's disease in the future.
As with all medications, dapansutrile has the potential to cause side effects. However, as it is still a relatively new medication, we can't yet be clear which side effects we can expect. In clinical trials to date, dapansutrile has been well tolerated with no serious reactions attributed to the medication.
There is a substantial time commitment associated with being part of a trial. We have minimised visits as much as possible to help with this.
Blood tests can cause minor discomfort and bruising of the skin. Standard protocols will be followed to reduce these risks, and to prevent infections. None of the blood tests in the trial will be fasting blood tests.
PET scans use a radioactive liquid (tracer) which is injected into the body to label certain cells in the brain so that we can see them on the scan. The tracer has short-lived radioactivity and there are no precautions for participants to take after the scan has been carried out. Like all medicines, injected tracers can be associated with some side effects. Side effects are rare and often relatively minor and short-lived but can include nausea, rash, abdominal discomfort, cold flushes and dizziness. Severe reactions are possible but are very rare and have never occurred in any of our own studies.
The PET scan uses ionising radiation to form images of the brain. Ionising radiation may cause cancer many years or decades after the exposure. We are all at risk of developing cancer during our lifetime. 50% of the population is likely to develop one of the many forms of cancer at some stage during their lifetime. Taking part in this trial will increase the chances of this happening from 50% to about 50.02%.
MRI scans involve a large magnet which is used to create high-quality pictures of the internal organs. Any metallic implants in the body will prevent a potential participant from taking part in this type of scan. We will go through a checklist to ask whether the participant has metal objects attached to or inside their body (e.g. stents, shrapnel, plated fractures, piercings, tattoos) or electronic devices (e.g. heart pacemaker). Many such items (most modern cardiac stents, for instance) are designed to be MRI-safe.
Participants will be asked to lie as still as they can in a small and enclosed space in the scanner for up to 90 minutes. Some participants may find this claustrophobic. The scanner is noisy, but participants will be given earplugs and/or headphones. Some patients might feel a bit dizzy or have a metallic taste in their mouth as they enter the scanner, but this will pass and we will be careful to make the scan as comfortable as possible. The technician performing the MRI scan will communicate with the participant throughout the scan to check that they remain comfortable. If needed, the scan can be stopped at any point.
There is a chance that scans may show a significant abnormality of which the participant is unaware. Similarly, in some cases blood tests, ECGs or our assessments may discover something about the participant's health that they are unaware of. In such circumstances, we would discuss the findings with the participant 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.
A possible side effect of a lumbar puncture is a headache, usually coming on within about 48 hours. Post-lumbar puncture headaches have been reported to occur in up to 1 in 4 people, but

more recent studies using modern methods show much lower rates, of around 1 in 20 people. The risk may be reduced by drinking plenty of fluids (a litre of water a day until the following day). If a headache does develop, it usually responds well to resting in bed, paracetamol and caffeine-containing drinks. For the lumbar puncture itself, we use local anaesthetic, but there may still be a feeling of pressure in the lower back at the time of the procedure, or mild tenderness or pain afterwards, which settles after a short time. Occasionally, there may be a little bleeding from the puncture site, as sometimes happens after a routine blood sample is taken. Rarely, some bruising or swelling at the site may occur. Serious complications after a lumbar puncture are extremely rare. These rare complications include tingling and numbness in the legs, infection in the spine, double vision, tinnitus and hypersensitivity to light or sound, but these are so rare as to be unquantifiable.
All risks are outlined in the participant information sheet and discussed with the participant as part of the consent process.

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?
January 2025 to March 2027

Who is funding the study?
Cure Parkinson's Trust (UK)

Who is the main contact?
Dr Caroline Williams-Gray, cuh.dapa-pd.trial@nhs.net

Contact information

Type(s)
Scientific, Principal investigator

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Dr Caroline Williams-Gray

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)

1010807

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CCTU0443

Study information

Scientific Title
Anti-inflammatory Intervention with dapansutrile (OLT1177®) for Parkinson’s disease modification (DAPA-PD): a randomised double-blind, placebo-controlled Phase II trial

Acronym
DAPA-PD

Study objectives
The primary objective is to evaluate the safety and tolerability of dapansutrile administered twice daily as adjunctive treatment with dopaminergic treatment in people with early PD.

The secondary objectives are:
1. To evaluate pharmacodynamics in the form of target engagement as determined by [18F]-DPA-714 PET neuroimaging, and blood and cerebrospinal fluid (CSF) markers of inflammation.
2. To evaluate the pharmacokinetics of dapansutrile in this patient population (plasma and CSF levels).
3. To evaluate the effect of dapansutrile administered twice daily on clinical outcome measures of motor and non-motor symptoms and quality of life in people with PD on a stable dose of dopaminergic medication.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 07/03/2025, London - City and East Research Ethics Committee (Research Ethics Committee Centre, 2nd Floor, 2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; -; cityandeast.rec@hra.nhs.uk), ref: 25/LO/0097

Study design
Open randomized double-blind placebo-controlled trial

Primary study design
Interventional

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Parkinson's disease

Interventions
Experimental research arm: Dapansutrile tablets administered for 26 weeks, starting at 1,000 mg daily (500 mg twice daily) for 4 weeks, escalating to 2,000 mg daily (1,000 mg twice daily) thereafter (if there are no safety or tolerability concerns).
Placebo comparator arm: Matched placebo tablets administered for 26 weeks, administered as per the active treatment.

Randomisation will be performed using Sealed Envelope (in a 2:1 ratio dapansutrile:placebo).

Participants will also be given the option to continue into an optional open-label phase of the trial, where they would receive dapansutrile treatment for an additional 26 weeks. In the open-label phase of the trial, dapansutrile will be started at 1,000 mg daily (500 mg twice daily) for 4 weeks, escalating to 2,000 mg daily (1,000 mg twice daily) thereafter (if there are no safety or tolerability concerns).

Intervention Type
Drug

Phase
Phase II

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

Primary outcome(s)
The number of adverse events (AEs) recorded during the 6-month double-blind treatment period, assessed at screening, baseline, day 1, and weeks 2, 4, 6, 12, 18, 23 and 26

Key secondary outcome(s))
1. Change in [18F]-DPA-714 non-displaceable binding potential (BPND) in subcortical and cortical regions of interest between baseline and week 23.
2. Change in levels of inflammatory biomarkers in blood including hsCRP, IL-1β, IL-18, IL-6, interferon (IFN)-gamma, tumour necrosis factor (TNF)-alpha, ASC specks over 6 months of treatment, measured at day 1, and weeks 6, 18 and 26.
3. Change in levels of inflammatory biomarkers in CSF including hsCRP, IL-1β, IL-18, IL-6, IFNgamma, TNF-alpha, ASC specks over 6 months of treatment, measured at baseline and week 26.
4. Pharmacokinetics as measured by changes in plasma dapansutrile concentrations and population pharmacokinetic (PK) parameters between baseline and end of treatment, measured at day 1, and weeks 6, 18 and 26. CSF levels will also be measured in select participants, at baseline and week 26

Completion date
31/03/2027

Eligibility

Key inclusion criteria
1. Have given written informed consent to participate
2. Be aged between 50 and 80 years (inclusive) at the time of the screening visit

3. Be a fluent English speaker
4. Have a diagnosis of clinically established early Parkinson's disease (PD) according to the Movement Disorder Society Criteria for Clinically Established Early Parkinson’s Disease
5. Have a disease duration of less than 5 years at the time of screening visit
6. Have early-stage PD, defined as Hoehn and Yahr stage ≤2
7. Be PD drug naïve or be receiving a stable dose of dopaminergic therapy for at least 3 months prior to the screening visit, or between screening and baseline
8. Have high sensitivity C-reactive protein (hsCRP) >1 mg/L at screening visit
9. Have adequate organ function, as defined below (to be rechecked prior to baseline /investigational medicinal product [IMP] initiation if >42 days from screening visit):
9.1. Haemoglobin ≥110 g/L
9.2. Platelet count ≥130 × 10^9/L
9.3. Neutrophil count ≥1.5 × 10^9/L
9.4. Renal function: estimated glomerular filtration rate (eGFR) >45 mL/min/1.73m^2
9.5. Hepatic function: alanine aminotransferase (ALT) and bilirubin < 1.5 times the institutional upper limit of normal
9.6. Thyroid stimulating hormone (TSH) within normal range
9.7. Corrected calcium ≤ institutional upper limit of normal
9.8. Alkaline phosphatase (ALP) < 1.5 times the institutional upper limit of normal

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
50 years

Upper age limit
80 years

Sex
All

Key exclusion criteria
1. Low affinity binder for TSPO ligands based on genotyping for single nucleotide polymorphism (SNP) rs6971.
2. Any use of immunomodulatory drugs or biologic agents (such as azathioprine, mycophenolate, methotrexate, ciclosporin, cyclophosphamide etc.) within 12 months prior to screening visit, or between screening and baseline.
3. Any previous use of rituximab or alemtuzumab at any time.
4. Treatment with oral corticosteroids for greater than 2 weeks within 12 months prior to screening visit, or any oral or injected steroid use within 3 months prior to screening visit, or between screening and baseline.
5. Regular use of non-steroidal anti-inflammatory drugs (NSAIDs) – including aspirin >75 mg, naproxen, ibuprofen and meloxicam – on more than 2 days per week.
6. Known inflammatory or autoimmune disease.

7. Chronic or latent infection.
8. Severe infection requiring the use of parenteral antimicrobial agents within 2 months prior to screening visit, or between screening and baseline.
9. Skin, solid organ or haematological malignancy within the 5 years prior to screening visit, or between screening and baseline.
10. The inability to take or swallow oral medication.
11. Parkinson's Disease Dementia according to Movement Disorder Society (MDS) PD Dementia criteria.
12. A known genetic mutation associated with PD.
13. A positive test for human immunodeficiency virus (HIV), hepatitis B (HBV)/C (HCV) or syphilis.
14. Chronic liver disease.
15. Any concurrent medical or psychiatric condition or disease that is likely to interfere with the trial procedures or results, or that in the opinion of the investigator, would constitute a hazard for participating in this trial.
16. Women of childbearing potential – female participants must be surgically sterile or be post-menopausal. A post-menopausal state is defined as no menses for 12 months without an alternative medical cause.
17. Male participants must be surgically sterile or must agree to use effective contraception (as specified in the trial protocol) during the period of therapy and for 6 months after the last dose of the trial treatment.
18. Known hypersensitivity to dapansutrile or its excipients.
19. Received an investigational drug or used an invasive investigational medical device within 12 weeks before the screening assessment, or is currently enrolled in another interventional investigational trial. Participants currently enrolled in other observational studies may be recruited.
20. Contraindications to PET-magnetic resonance imaging (MRI) scanning including metal implants, claustrophobia or inability to lie flat for 90 minutes.
21. Concomitant treatment with any medications that could interfere with [18F]-DPA714 binding (e.g., benzodiazepines).
22. Current use of any drugs of abuse or average alcohol intake of >21 units per week over the last 3 months.
23. Any other significant disease, disability or investigation result which, in the opinion of the Chief Investigator (CI), 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
01/02/2025

Date of final enrolment
31/03/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre

Addenbrookes
Addenbrookes Hospital
Hills Road
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CB2 0QQ

Sponsor information

Organisation
Cambridge Clinical Trials Unit

Funder(s)

Funder type
Charity

Funder Name
Cure Parkinson's Trust

Alternative Name(s)
The Cure Parkinson's Trust, CPT

Funding Body Type
Government organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

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