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Investigating 4’PPT for pantothenate kinase associated neurodegeneration (PKAN)

Submission date
21/02/2025

Recruitment status
No longer recruiting

Registration date
21/03/2025

Overall study status
Ongoing

Last Edited
08/04/2026

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
Pantothenate kinase-associated neurodegeneration (PKAN) is a rare but devastating fatal condition that affects the brain. Children are born normally but progressively lose the ability to walk or talk and develop painful twisting movements called dystonia. Children with PKAN cannot convert vitamin B5 into an essential molecule called co-enzyme A.
There are currently no treatments that change the course of this progressive disease, leading to major disability and a high risk of death in childhood. This study will investigate a new vitamin metabolite designed to correct the metabolic problem causing the disease by giving a partially processed form of vitamin B5 called 4’-phosphopantetheine (called UK-PKAN-B5D).

Who can participate?
Young people aged between 1 and 25 years

What does the study involve?
Participants will be randomly allocated to take UK-PKAN-B5D by mouth or feeding tube daily for 24 weeks followed immediately by a 24-week open-label phase. Safety measures will include monitoring of all adverse events, regular safety blood tests, and the use of PKAN-specific activities of daily living and disease rating scales. Exploratory outcomes will assess biomarkers in blood, eye testing to monitor PKAN eye disease, and quality of life and dystonia.

What are the possible benefits and risks of participating?
The aim of this study is to ensure that this medicine is safe and well tolerated by participants with no significant side effects. In the longer term, the researchers plan to develop this as a food for special medical purposes for the dietary management of patients with PKAN. This study product is low risk with no evidence of toxicity from animal or other human studies.

Where is the study run from?
Great Ormond Street Hospital for Children (UK)

When is the study starting and how long is it expected to run for?
September 2020 to March 2027

Who is funding the study?
1. Great Ormond Street Children's Charity (UK)
2. LifeArc (UK)

Who is the main contact?
Prof. Manju Kurian, manju.kurian@ucl.ac.uk

Contact information

Type(s)
Public, Scientific, Principal investigator

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Prof Manju Kurian

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Additional identifiers

Integrated Research Application System (IRAS)
1003863

Protocol serial number
19NM10 (Sponsor protocol number)

Study information

Scientific Title
A Phase II study of a novel vitamin metabolite for pantothenate kinase associated neurodegeneration (PKAN)

Study objectives
4-phosphopantetheine (4-PPT) will be safe and tolerable for patients affected by pantothenate kinase-associated neurodegeneration (PKAN), an inborn error of
vitamin B5 metabolism.

Ethics approval required
Ethics approval required

Ethics approval(s)

Approved 24/06/2024, South Central - Oxford C Research Ethics Committee (Health Research Authority, 2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 1048144; oxfordc.rec@hra.nhs.uk), ref: 24/SC/0179

Primary study design
Interventional

Study design
Phase II single-centre study with an initial 24-week randomized, double-blind, placebo-controlled phase followed by a 24-week, open-label phase of a product containing 4-PPT in UK patients

Study type(s)
Safety, Other

Health condition(s) or problem(s) studied
Pantothenate kinase-associated neurodegeneration (PKAN)

Interventions
Study product: UK-PKAN-B5D (capsule containing 4-phosphopantetheine [4-PPT]) or matched placebo). To be dosed enterally once per day.

Participants will take UK-PKAN-B5D by mouth or feeding tube daily for a 24-week randomized, double-blind, placebo-controlled phase followed immediately by a 24-week open-label phase.

Intervention Type
Other

Primary outcome(s)
The long-term safety and tolerability profile of 4-PPT measured using:
1. Incidence of adverse events and serious adverse events during the 24-week placebo-controlled phase, comparing active and placebo groups
2. Incidence of adverse events and serious adverse events over the full 48-week period, including standard laboratory tests

Key secondary outcome(s)
The safety of 4-PPT measured using PKAN disease-specific scales over the 24-week placebo-controlled phase of active and control groups:
1. PKAN Activities of Daily Living (PKAN-ADL)
2. PKAN Disease Rating Scale (PKAN-DRS)

Completion date
31/03/2027

Eligibility

Key inclusion criteria
1. Confirmed PKAN diagnosis: bi-allelic pathogenic PANK2 mutations OR a single pathogenic PANK2 mutation and typical findings on history, exam and brain MRI:
1.1. Classic PKAN: motor symptom onset under 5 years of age (if recruited at under 10 years of

age) OR loss of independent ambulation by age 10 years (if 10 years or over at recruitment)
OR
1.2. Atypical PKAN: all other PKAN patients who do not meet the criteria for classic PKAN
2. Older than 12 months of age and under 25 years of age at the time of screening
3. Able to take study product by mouth or enterally by nasogastric/gastrostomy tube
4. Able and willing to travel for, and complete study procedures
5. Be already enrolled or willing to enrol in the 'PKAN-ready' natural history study (eIRB10832)
6. Female participants of childbearing potential (who have begun menstruation) must have a negative pregnancy test result at the Screening Visit. In addition, if applicable, females of childbearing potential must use a highly effective method of contraception according to local requirements (see below)
7. UK resident for study duration

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
12 Months

Upper age limit
25 Years

Sex
All

Total final enrolment
15

Key exclusion criteria
1. Exposed to another PANK2 'bypass' agent less than 4 months prior to screening. These would include any agent aiming to bypass the loss of PANK2 enzyme activity
2. Enrolled in another interventional clinical study or received another Investigational Medicinal Product in the 4 months prior to screening
3. Deep brain stimulation implantation planned within 6 months from study enrolment
4. Have co-existing medical conditions that preclude completion of study procedures or confound assessment of clinical/laboratory safety measures
5. Pregnant or breastfeeding
6. Known galactosaemia or severe hypersensitivity to lactose

Date of first enrolment
29/04/2025

Date of final enrolment
16/01/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Great Ormond Street Hospital for Children
Great Ormond Street
London
England
WC1N 3JH

Sponsor information

Organisation
Great Ormond Street Hospital for Children NHS Foundation Trust

ROR
https://ror.org/00zn2c847

Funder(s)

Funder type
Charity

Funder Name
LifeArc

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Funder Name
Great Ormond Street Hospital Charity

Alternative Name(s)
Great Ormond Street Hospital Children's Charity, GOSH Charity, greatormondSt, GOSH

Funding Body Type
Private sector organisation

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

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 available upon request from Prof. Manju Kurian (manju.kurian@ucl.ac.uk)

IPD sharing plan summary
Available on request