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Practicality of carrying out a clinical trial of early Levodopa treatment for improving eyesight in children with albinism

Submission date
21/02/2023

Recruitment status
Not yet recruiting

Registration date
19/08/2026

Overall study status
Ongoing

Last Edited
19/08/2026

Condition category
Nutritional, Metabolic, Endocrine

[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
Currently, there are no treatments for the eye problems seen in albinism (oculocutaneous albinism). The average vision in albinism at 20/80, is below UK driving standards, which has implications for school, work and social life. This is why finding a treatment that can improve eyesight in albinism, was named a priority by the Sight Loss and Vision Priority Setting Partnership in 2013. We know that the brain has the amazing ability to change and adapt in children. We also know that we make use of the brain's ability to rewire itself when we improve eyesight in lazy eyes using glasses and patching. In albinism, a chemical called L-DOPA is missing from the eye and this causes problems with eye development. This is why eyesight is so poor in albinism. However, the eye is still able to change and develop in young children with albinism. Similar to the treatment of lazy eyes, we can target this flexibility in albinism. Potentially, replacing L-DOPA in albinism at a young age will improve eye development and eyesight. The aim of this study is to carry out a small trial of L-DOPA treatment in children with albinism. L-DOPA is a safe medicine that is currently being used to treat infants and young children born with problems controlling the movement of their limbs.

Who can participate?
Children aged between 3 and 18 months with a diagnosis of oculocutaneous albinism

What does the study involve?
We will explore, together with the parents of the affected children, if the treatment and examinations carried out as part of this trial are reasonable. If successful, this study will completely change how children with albinism are treated. It will also set an important precedent for the development of new treatments for other eye diseases that affect children.

What are the possible benefits and risks of participating?
1. Potential Side Effects from the study drug
Children may experience side effects such as nausea and vomiting (usually within two hours of taking a dose). In order to reduce this risk, the Levodopa dose selected for this study is based on recommendations obtained from:

1.1. The British National Formulary for Children,
1.2. The Guys and St Thomas Paediatric Formulary and
1.3. The existing evidence base for its use in infants and children with: 1.3.1. Infantile dystonia (a type of movement disorder), 1.3.2. Defects in tetrahydrobiopterin synthesis and dihydrobiopterin reductase deficiency (metabolic disorders), 1.3.3. Albinism and 1.3.4. Amblyopia (lazy eye). Levodopa will be given with Carbidopa, as this is known to be effective in limiting Levodopa-related side effects such as nausea, vomiting and cardiovascular adverse drug reactions. The 1st dose will also be administered at the randomisation visit and the participant will be observed for at least two hours for any adverse reactions. The drug will only be dispensed if this is tolerated. Children and their carers will be warned of the risk of mood disorders, excessive daytime sleepiness and sudden onset of sleep. All participants will be monitored for the development of movement disorders, which will be managed by decreasing their L-DOPA dose. Furthermore, as this is a short (20-week) course of treatment, the long-term problems e.g. dyskinesias (an involuntary movement disorder) observed with Levodopa use in Parkinsonism are not expected. The study team includes a consultant paediatric neurologist who is highly experienced in neurodevelopment and routinely prescribes Levodopa to treat infants and young children with other neurological conditions. A reduction in dosage or termination of therapy may be considered if the participant develops and cannot tolerate side effects associated with Levodopa.

2. Potential complications from abrupt Levodopa withdrawal.
A syndrome resembling the neuroleptic malignant syndrome has been reported with the abrupt withdrawal of antiparkinsonian agents. In order to address this issue, the study protocol stipulates that dose reductions will gradually take place every 2-3 days over the course of a week.

3. Risk of overdoses
Levodopa overdose is associated with the development of heart rhythm abnormalities. In order to manage an acute overdose, ECG monitoring will be instituted, and the patient carefully observed for the possible development of arrhythmias; if required, appropriate anti-arrhythmic therapy will be given.

5. This protocol requires additional appointments and procedures over and above those which would be expected from standard care. These are necessary in order to ensure that the drug effects are evaluated in sufficient detail to ensure the safety of the participants and to generate the data needed to plan a definitive treatment trial in the future. In consultation with our PPI group, we have designed the study visit schedule in order to minimise the burden of visits and procedures on the participant and their families. Appointments and procedures will be scheduled to coincide with the follow-up visits that would typically occur as part of standard clinical care. Participants will be compensated for their travel costs. Furthermore, the acquisition protocols for each procedure in this study have been designed in order to ensure rapid and reliable data acquisition, whilst minimising any potential distress to the participants.

6. Blood testing (Required to ensure no toxic effects from the drug).
Many children and their parents feel anxious at the thought of having a blood test. This will be alleviated through the provision of an information leaflet about the procedure before it is carried out (i.e. http://www.uhs.nhs.uk/Media/Controlleddocuments/Patientinformation /Childhealth/Having-a-blood-test-or-cannula.pdf). Blood sampling will be performed by a specially trained paediatric nurse. In order to reduce any pain or discomfort experienced by the child during blood sampling, numbing cream or cold spray can be offered to numb the skin.

Where is the study run from?
Southampton University Hospital (UK)

When is the study starting and how long is it expected to run for?
August 2026 to April 2028.

Who is funding the study?
Medical Research Council (MRC)

Who is the main contact?
Dr Helena Lee, helena.lee@soton.ac.uk (UK)

Contact information

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Additional identifiers

Clinical Trials Information System (CTIS)
2019-004484-44

Integrated Research Application System (IRAS)
1006076

Protocol serial number
RHM OPH0276

Study information

Scientific Title
Feasibility of a phase III randomised controlled trial of oral levodopa treatment in improving visual development in infants and young children with albinism: a small pilot study of 10 patients

Acronym
The OLIVIA study

Study objectives
To begin exploring the feasibility of the intervention, measurement and trial procedures, for a future phase IIIa randomised controlled trial (RCT) to test the safety and efficacy of oral L-DOPA (Levodopa) supplementation in improving visual development in infants and young children with albinism.

None planned as this is a small exploratory pilot feasibility study of 10 patients, which is not intended to confirm efficacy of the treatment.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 07/08/2026, Health and Social Care Research Ethics Committee A (HSC REC A), Office for Research Ethics Committees Northern Ireland (ORECNI). (Office for Research Ethics Committees Northern Ireland (ORECNI) 2nd Floor James House 2-4 Cromac Avenue, Belfast, BT7 2JA, United Kingdom; +44 28 95 361400; info.orecni@hscni.net.), ref: 26/NI/0064

Primary study design
Interventional

Study design
Randomized placebo-controlled double-blind study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Oculocutaneous albinism

Interventions
Participants aged 3 to 18 months with oculocutaneous albinism will be enrolled into a single-centre, double-masked, placebo-controlled pilot feasibility study. Participants will be randomised using blocked randomisation in a 4:1 ratio to one of the following arms:

Active treatment arm: Oral Levodopa-Carbidopa (0.76-1.0 mg/kg levodopa with 25% carbidopa) administered three times daily for 20 weeks. Treatment will begin at a lower once-daily dose and be titrated every 2-3 days during the first week to the target dose. Following completion of treatment, the medication will be tapered over approximately one week.

Control arm: Matching oral placebo administered according to the same schedule for 20 weeks. The first dose will be administered under supervision at the randomisation visit, with observation for adverse reactions. Participants will subsequently undergo scheduled safety monitoring, telephone reviews, and study visits over a 12-month follow-up period.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Levodopa-Carbidopa capsules

Primary outcome(s)
1. Feasibility of eligibility criteria, assessed by the specificity and sensitivity of the proposed diagnostic criteria throughout recruitment and study completion
2. Number of potentially eligible participants, recorded using screening logs during the recruitment period
3. Evaluation of recruitment and retention processes assessed as follows:
4. Recruitment and retention feasibility, assessed by:
4.1. Percentage of contacted families participating in the study
4.2. Percentage of participants compliant with treatment and follow-up
4.3. Percentage of participants stopping treatment because of side effects
4.4. Percentage of participants withdrawing and reasons for withdrawal
4.5. Percentage of participants completing 12-month follow-up
5. Acceptability of trial procedures, assessed through semi-structured interviews exploring recruitment processes and acceptability of treatment and study procedures at 6 months
6. Assessment feasibility, measured by:
6.1. Percentage successfully completing each assessment
6.2. Acquisition speed and reliability of assessments
6.3. Robustness of trial procedures
6.4. Number of inadvertent unmasking events
7. Safety, assessed by the total number and type of adverse events recorded throughout the study

Key secondary outcome(s)
There are no secondary outcome measures

Completion date
28/04/2028

Eligibility

Key inclusion criteria

Children aged between 3 and 18 months with a diagnosis of oculocutaneous albinism (OCA) based on previously established diagnostic criteria as follows:
1. 3 major criteria or
2. 2 major and 2 minor criteria for the diagnosis of albinism or
3. In the presence of a molecular diagnosis, 1 major criterion or 2 minor criteria for the diagnosis of albinism will be sufficient.

Major criteria
1. Foveal hypoplasia grade 2 or more
2. Optic nerve misrouting on visual evoked potential (VEP) testing
3. Ocular hypopigmentation, either Iris transillumination defects or fundus hypopigmentation grade 2 or more

Minor criteria
1. Infantile nystagmus
2. Cutaneous hypo-pigmentation
3. Grade 1 fundus hypopigmentation

Molecular diagnosis
1. A genotype consisting of 1 previously published pathogenic variant in a known OCA gene or 1 novel variant deemed 'highly likely' to be pathogenic & either
2. A 2nd known or novel 'highly likely' pathogenic variant in the same gene or
3. A 2nd common variant in the same gene, known to be associated with an albino phenotype

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Diagnosis of ocular albinism (OA1) as the OA1 receptor needs to be intact in order for L-DOPA treatment to be effective
2. Ocular abnormalities other than those associated with OCA
3. Any pre-existing neurological or metabolic abnormalities that may affect ocular development
4. Severe cardiovascular or pulmonary disease, bronchial asthma, renal, hepatic or endocrine disease
5. Any significant medical or surgical conditions that would risk the patient’s safety or their ability to complete the trial
6. Demonstrations of a clinically significant deviation in any of the following laboratory parameters at baseline:
6.1. Full blood count

6.2. Renal function
6.3. Bone profile
6.4. Liver function
7. Children of parents who do not consent will not be enrolled into the study

Date of first enrolment
31/08/2026

Date of final enrolment
31/08/2027

Locations

Countries of recruitment
United Kingdom

Study participating centre
University Hospital Southampton NHS Foundation Trust
Southampton General Hospital
Tremona Road
Southampton
England
SO16 6YD

Sponsor information

Organisation
University Hospital Southampton NHS Foundation Trust

ROR
https://ror.org/0485axj58

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council

Alternative Name(s)

Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Individual participant data generated during this study will be available from the Chief Investigator upon reasonable request following publication of the primary study results, subject to appropriate ethical approvals, data sharing agreements, and applicable data protection regulations. Only de-identified participant data will be shared. Data access requests will be reviewed by the Trial Steering Committee and approved requests will be subject to a formal Data Sharing Agreement. Participant consent for data sharing will be obtained at enrolment. Study data will be retained for a minimum of 25 years.

IPD sharing plan summary
Available on request