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Gene therapy for treatment of choroideremia

Submission date
18/04/2016

Recruitment status
No longer recruiting

Registration date
28/04/2016

Overall study status
Completed

Last Edited
05/06/2024

Condition category
Eye Diseases

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

Plain English summary of protocol

Background and study aims
Choroideremia is a rare incurable inherited disorder that almost exclusively affects males. It causes progressive loss of vision (sight) due to degeneration of the choroids (cells that are essential for sight) and retina (light-sensitive area at the back of the eye). The disease is caused by a defect in a certain gene located on the X-chromosome (i.e. the sex chromosome), and this is why the disease affects men and women differently. Women have two X-chromosomes and so a normal gene on one X-chromosome can compensate for a defective gene on the other X-chromosome to some extent. Men, however, only have one X-chromosome. Sight loss in choroideremia begins with 'night blindness' (i.e. loss of night vision) in adolescence, followed by a gradual loss of peripheral vision which results in progressively worsening 'tunnel vision'. Ultimately, central vision is lost by the fourth or fifth decade. There are currently no treatments available that can successfully treat choroideremia, but a new gene therapy technique has been developed which may help to slow or even stop the degeneration. The new technique involves putting normal copies of the affected gene back into the cells of the retina to help them to function normally. This is achieved by an operation to inject the normal genes into the retina, using a modified virus to carry the genes into the cells. The purpose of this study is to find out if vision can be preserved in patients suffering from choroideremia by replacing the defective gene using gene therapy. This study is the continuation of an earlier one which started in 2011, and which has shown encouraging results so far.

Who can participate?
Men aged at least 18 with choroideremia.

What does the study involve?
One eye of each participant in the study is treated with the gene therapy. This includes a surgical procedure where normal copies of the defective genes that cause choroideremia are injected into the retina. Each participant is then followed up over the next 24 months, comparing disease progression of the treated eye compared to the untreated one. The decision about which eye to treat is on clinical grounds and is generally the worse eye affected. The eye to be treated is randomised in cases where the degeneration is about the same in both eyes.

What are the possible benefits and risks of participating?
Possible benefits include the slowing down or possibly preventing further loss of sight in men affected by choroideremia. Side effects of the surgical procedure may include, pain and

discomfort, infection or, more rarely, tearing or detachment of the retina and haemorrhage. Possible side effects of the gene therapy include inflammation or, more rarely, a severe immune response.

Where is the study run from?
1. Oxford Eye Hospital (UK)
2. Moorfields Eye Hospital, London (UK)

When is the study starting and how long is it expected to run for?
May 2016 to December 2020

Who is funding the study?
1. National Institute for Health Research (UK)
2. Medical Research Council (UK)

Who is the main contact?
Dr Marco Bellini

Contact information

Type(s)
Public

Contact name
Dr Marco Bellini

Contact details
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Additional identifiers

Clinical Trials Information System (CTIS)
2015-001383-18

ClinicalTrials.gov (NCT)
NCT02407678

Protocol serial number
CPMS 19780

Study information

Scientific Title
An open label Phase 2 clinical trial of retinal gene therapy for choroideremia using an adeno-associated viral vector (AAV2) encoding Rab-escort protein 1 (REP1)

Acronym
REGENERATE

Study objectives
The aim of this study is to find out if it is possible to preserve vision in patients suffering from choroideremia by replacing the defective gene using gene therapy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London - West London & GTAC Research Ethics Committee, 16/10/2015, ref: 15/LO/1379

Study design
Randomized; Interventional; Design type: Treatment, Gene Therapy

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
AAV2.REP1, Adeno-associated viral vector (AAV2) encoding Rab-escort protein 1 (REP1)

One eye will receive the gene therapy. The efficacy of the gene therapy will be evaluated by comparing the progress of the disease over a period of 24 months in the treated eye and the untreated control eye. The decision about which eye to treat will be made on clinical grounds and will generally be the worse eye affected. The eye to be treated will be randomised in cases where the degeneration is relatively symmetrical between the two eyes.

Intervention Type
Other

Primary outcome(s)
Change in best corrected visual acuity in the treated eye, assessed at baseline, day 7, month 1, month 3, month 6, month 9, month 12, month 18 and month 24

Key secondary outcome(s))
Change from baseline in other functional, immunological, physiological and anatomical outcomes in the treated eye pertaining to vector efficacy and safety, and safety of the surgical procedure

Completion date
31/07/2021

Eligibility

Key inclusion criteria
1. Willing and able to give informed consent for participation in the study
2. Male aged 18 years or above
3. Genetic or molecular confirmed diagnosis of choroideremia (REP1 protein deficiency)
4. Active disease visible clinically within the macula region
5. Best corrected visual acuity equal to or worse than 6/6 (20/20; Decimal 1.0; LogMAR 0) but better than or equal to 6/60 (20/200; Decimal 0.1; LogMAR 1.0) in the study eye

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Male

Total final enrolment
30

Key exclusion criteria
1. Any female, or a male aged below 18 years
2. An additional cause for sight loss (e.g. amblyopia) in the eye to be treated
3. Any other significant ocular and non-ocular disease or disorder which, in the opinion of the investigator, may put the participants at risk because of participation in the study
4. Inability to take systemic prednisolone for a minimum of 3 weeks
5. Unwillingness to use barrier contraception methods for a period of three months following gene therapy surgery, if relevant
6. Participation in another research study involving an investigational product in the preceding 12 weeks

Date of first enrolment
01/05/2016

Date of final enrolment
30/06/2019

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Oxford Eye Hospital
Lower Ground 1
West Wing
John Radcliffe Hospital
Oxford
United Kingdom
OX3 9DU

Study participating centre
Moorfields Eye Hospital
162 City Road
London
United Kingdom
EC1V 2PD

Sponsor information

Organisation
NIHR Evaluation, Trials and Studies Coordinating Centre (NETSCC)

ROR
https://ror.org/03d7d0579

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available as the data has been licensed to a biotech company, Nightstar Therapeutics (the supplier of the gene therapy being tested in this study), for their use in a future submission for regulatory approval.

IPD sharing statement
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IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/05/2024	05/06/2024	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol (other)		08/07/2020	23/08/2022	No	No