ISRCTN51772481 https://doi.org/10.1186/ISRCTN51772481

To evaluate the safety and effectiveness of human ex vivo expanded autologous limbal stem cells for the treatment of unilateral total limbal stem cell deficiency

Submission date
27/04/2012

Recruitment status
No longer recruiting

Registration date
27/04/2012

Overall study status
Completed

Last Edited
30/01/2023

Condition category
Eye Diseases

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

Plain English summary of protocol

Background and study aims
The cornea is the clear window at the front of the eye. It allows light to enter the eye and helps to focus the light in the back of the eye. In order for us to see a clear image, the cornea has to be transparent, regular and smooth. The outer layer of the cornea is called the epithelium and this is made of epithelial cells. Healthy corneal epithelial cells are transparent (allow light to pass through) and are arranged in regular layers. Most epithelial cells have less ability to multiply themselves. However, there are also special stem cells in the cornea (limbal stem cells) that are able to multiply over and over again, acting like a reservoir that can endlessly produce new epithelial cells. They also prevent the conjunctival epithelium (covering the white part of the eye) from growing over the cornea. If the stem cells are diseased or damaged by chemical burns or disease, a condition occurs called limbal stem cell deficiency (LSCD). The corneal epithelium often breaks down, causing discomfort and pain. Conjunctival epithelium grows onto the cornea, blocking out the light, causing reduced vision. In order to improve the condition, the patient can be given more stem cells by having a treatment called a limbal stem cell transplant. Limbal stem cells can be taken from the other eye if it is healthy, or sometimes from a relative or donor. However, removing many stem cells from the good eye (about a third of the total number would be necessary) could cause stem cell deficiency in that eye as well. A solution to this problem is to remove only a few stem cells from the good eye and then to grow these cells under germ-free conditions in a special laboratory. The increased number of cells can then be placed into the diseased eye. The aim of this study is to treat the limbal stem cell deficiency by transplanting limbal stem cells from the healthy other eye which have been grown in a laboratory.

Who can participate?
Men and women aged 18 or over, with limbal stem cell deficiency in one eye (the other eye must be healthy).

What does the study involve?
A small amount of tissue is taken from the healthy eye. The tissue sample will be grown in the

laboratory for approximately 14 days. There should then be enough stem cells to use for the treatment. The grown stem cells will be placed and stitched on to the surface of the diseased eye. Please note that these operations cannot be reversed once done, even if the patient decides to stop taking part in this study. The condition of the eye and symptoms will be checked at all visits. For the purpose of the study we will perform several tests, although not all will be done at every visit. Many of the procedures will be familiar to the patient as a part of ongoing treatment. There are also other new tests and investigations that will be performed.

What are the possible benefits and risks of participating?
We cannot promise that the study will help the patient but we hope the treatment will be successful. If it is, then the visual symptoms and/or vision will improve and the condition will become more comfortable. Information we get from this study will help improve the treatment of many more people with limbal stem cell deficiency. For any eye treatment or operation, there is always a degree of risk. We have reduced these where possible by using a number of safe practices, testing and making sure that our study procedures are approved by concerned authorities. Since this is a research study and the techniques are not widely used yet, there may be other unforeseen risks or longer term risks which have not been identified yet.

Where is the study run from?
The Newcastle upon Tyne Hospitals NHS Foundation Trust (UK).

When is the study starting and how long is it expected to run for?
March 2012 to July 2014

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

Who is the main contact?
Professor Francisco C Figueiredo
f.c.figueiredo@ncl.ac.uk

Contact information

Type(s)
Scientific

Contact name
Ms Claire Macdonald

Contact details
Newcastle Clinical Trials Unit
Institute of Health & Society
Newcastle University
Newcastle Upon Tyne
United Kingdom
NE2 4HH
-
claire.macdonald@ncl.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2011-000608-16

Protocol serial number
11185

Study information

Scientific Title
To evaluate the safety and effectiveness of human ex vivo expanded autologous limbal stem cells for the treatment of unilateral total limbal stem cell deficiency: a non-randomised study

Study objectives
This is a single-centre prospective interventional case series phase II study to determine the efficacy and safety of ex vivo expanded autologous limbal stem cell transplantation to treat patients with total unilateral limbal stem cell deficiency. The primary objective is to evaluate the safety and efficacy of an animal free ex vivo expanded autologous limbal stem cells (LSC) transplantation for the treatment of unilateral total limbal stem cell deficiency (LSCD).

More details can be found at http://public.ukcrn.org.uk/search/StudyDetail.aspx?StudyID=11185

On 04/06/2014 the anticipated end date was changed from 30/11/2013 to 31/07/2014 .

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee North East Newcastle and North Tyneside 1, 16/08/2011, ref: 11/NE/0236

Study design
Non-randomised; Interventional; Design type: Treatment

Primary study design
Interventional

Study type(s)
Screening

Health condition(s) or problem(s) studied
Topic: Eye; Subtopic: Eye (all Subtopics); Disease: Ophthalmology

Interventions
Ex vivo expanded autologous LSC, the technique involved taking a small limbal biopsy from the healthy other eye of each patient with unilateral total LSCD and expanding the LSC population ex vivo on to Human Amniotic Membrane (HAM) and then transplanting this enlarged population into the prepared disease eye (i.e., superficial keratectomy) combined with a second HAM (stroma facing down) on top as a biological bandage.

Intervention Type
Other

Phase
Phase II

Primary outcome(s)
Reversal of LSCD by impression cytology; Timepoint(s): 6, 12, 24 and 36 month post-op

Key secondary outcome(s))
1. Corneal opacity assessment by anterior segment OCT; Timepoint(s): all visits post-op up to 36 months
2. Corneal/limbal epithelial assessment by confocal microscopy; Timepoint(s): 6, 12, 18, 24 and 36 months post-op
3. Improvement in LogMAR Visual acuity; Timepoint(s): all visits post-op up to 36 months
4. Improvement in patients reported ocular surface pain; Timepoint(s): 12 weeks, 6, 12, 18, 24 and 36 months post-op
5. Improvement in patients reported outcomes; Timepoint(s): 12 weeks, 6, 12, 18, 24 and 36 months post-op
6. Ocular surface reconstruction (i.e., corneal re-epithelisation); Timepoint(s): all visits post-op up to 36 months
7. Presence of complications; Timepoint(s): all visits post-op up to 36 months
8. Reduction in corneal opacity; Timepoint(s): all visits post-op up to 36 months
9. Reversal in central corneal vascularisation; Timepoint(s): all visits post-op up to 36 months

Completion date
31/01/2018

Eligibility

Key inclusion criteria
1. Patient has provided written informed consent for participation in the study prior to any study-specific procedures
2. Patients must be 18 years of age or older and consent to have their data included in the database for research purposes
3. Patients must be prepared and able to complete questionnaires
4. Diagnosis of unilateral total LSCD (confirmed by impression cytology), with normal B scan ultrasound and electrophysiology
5. No other ocular abnormality in recipient eye(s)
6. Women of childbearing potential must be using adequate contraception for duration of study and have a negative baseline pregnancy test as part of screening (postconsent)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Significant comorbidity in which compliance with the study procedures would not be expected e.g. suspected insufficient cognitive ability to perform the tests (assessed using the 11-item Telephone Interview for Cognitive Status instrument)
2. Dry eye and eyelid abnormality in the affected eye
3. Previous surgery to the ocular surface of the healthy contralateral donor eye
4. Abnormal corneal impression cytology in the healthy contralateral donor eye
5. Pregnancy, or women planning to become pregnant within next 36 months, or women who are breastfeeding
6. Participating in other investigational study within 30 days prior to study entry (defined as date of enrolment/baseline visit into study)
7. Previous participation in this study

Date of first enrolment
06/03/2012

Date of final enrolment
31/10/2014

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Royal Victoria Infirmary
Department of Ophthalmology
The Newcastle upon Tyne Hospitals NHS Foundation Trust
Queen Victoria Road
Newcastle Upon Tyne
United Kingdom
NE1 4LP

Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust (UK)

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council (MRC) (UK)

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 current 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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		28/01/2023	30/01/2023	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes