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A first-in-human trial assessing the safety and efficacy of the RAFT transplant in the treatment of aniridia-related keratopathy

Submission date
18/02/2021

Recruitment status
Stopped

Registration date
11/03/2021

Overall study status
Stopped

Last Edited
21/06/2024

Condition category
Eye Diseases

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
The RAFT trial is a first in human trial of a new cellular treatment called RAFT-OS (Real Architecture for 3D Tissues Ocular Surface) developed and manufactured by Cells for Sight Stem Cell Therapy Research Unit at UCL institute of Ophthalmology.
The aim of the trial is to investigate if RAFT-OS is a safe and effective alternative treatment for patients with aniridia-related keratopathy (ARK) in 21 patients. ARK is a complication of aniridia, which is a genetic eye condition present from birth. Aniridia is a rare condition where the iris (the coloured part of your eye) has not formed properly, so it may be missing or underdeveloped. Keratopathy means disease of the cornea (the front part of the eyeball).
RAFT-OS is an artificial tissue, populated with cells from donated human corneas from the NHS blood and Transplant, Tissue and Eye services Liverpool.

Who can participate?
Men and women who are over 18 years of age and have a confirmed diagnosis of ARK which has progressed towards the centre of their eyes and is reducing their vision.

What does the study involve?
Participants will commence on 3 months of immune suppression therapy to prepare for the transplantation of RAFT-OS. The product will then be transplanted into the participants worst affected eye. Participants will then be followed up closely for the first 4 weeks following surgery for signs of infection or other complications. If there are no serious events, the next participant will be treated with RAFT-OS.
The trial team will regularly follow participants after transplantation for 12 months, with detailed review of symptoms, investigations such as digital photography of the eye and examinations of the surface of the eye.
Participants will be required to stay on the immune suppression therapy for the duration of the trial.

What are the possible benefits and risks of participating?
Potential benefits of taking part are helping us with the process of developing new treatments

for ARK, as there are currently no alternative treatments.
Possible risks of taking part are possible side effects from the surgical procedure, the trial treatment and the immunosuppression therapy.

Where is the study run from?
The study is run by the Comprehensive Clinical Trials Unit at UCL. The single site is Moorfields Eye Hospital in London (UK).

When is the study starting and how long is it expected to run for?
April 2019 to May 2025

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

Who is the main contact?
RAFT trial manager, raft@ucl.ac.uk

Study website
https://www.ucl.ac.uk/comprehensive-clinical-trials-unit/research-projects/2023/may/raft

Contact information

Type(s)
Scientific

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Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
2019-002371-34

IRAS number
269184

ClinicalTrials.gov number
NCT05044598

Secondary identifying numbers
CPMS 48192, IRAS 269184

Study information

Scientific Title
First in human phase I/II clinical trial of RAFT for aniridia-related keratopathy

Acronym
RAFT

Study objectives
The RAFT trial is a first in human trial of a novel cellular therapy called RAFT-OS (Real Architecture for 3D Tissues Ocular Surface) developed and manufactured by Cells for Sight Stem Cell Therapy Research Unit at UCL institute of Ophthalmology.
The aim of the trial is to investigate if RAFT-OS is a safe and effective alternative treatment for patients with aniridia related keratopathy (ARK) in 21 patients. ARK is a complication of aniridia, which is a genetic eye condition present from birth.
The hypothesis for the RAFT trial is that the replacement of 1) LESC, 2) stromal cells relevant to epithelium support and 3) a stroma (which is lacking in kerotolimbal-allografts), together in RAFT-OS, will be safe and improve cultured LESC therapy outcome in patients with ARK.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 19/04/2021, South Central Oxford A (Ground Floor Temple Quay House, 2 The Square, Bristol BS1 6PN, UK; +44 (0)207 104 8284; oxforda.rec@hra.nhs.uk), ref: 21/SC/0020

Study design
Interventional non-randomized

Primary study design

Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Damage to the cornea due to a complete or partial absence of the coloured part of the eye (aniridia-related keratopathy)

Interventions
This is a seamless phase I/II single-dose, single-arm safety and efficacy evaluation of RAFT-OS in patients with ARK.

A two-stage approach to in evaluating safety and efficacy will be taken.

Stage 1: Patients 1 to 9
For the first 6 patients there will be sequential recruitment with a minimum of 1 month between recruitment of each participant. Each participant will be assessed at days 1, 7, 14, 21, and 1 month post RAFT-OS transplantation for major or intermediate safety events. If one of these events occurs, the joint TSC and IDMC will be consulted before recruitment of the next patient.

After the first 6 patients have completed 1 month of follow-up, the joint TSC and IDMC will convene and review the safety data. They will then recommend how to proceed; sequential recruitment as, cohorts of two, full parallel recruitment, or stopping the trial. The recommendation will be based on pre-specified stopping and adaptation rules outlined in this document and other relevant patient outcome data. If recruitment proceeds in any form, after 9 patients have completed 3 months follow up the joint TSC and IDMC will meet and again decide whether to stop, maintain, accelerate or decelerate recruitment, using stopping and adaptation rules based on the available safety and efficacy data for the first 9 patients.

Stage 2: Patients 10 to 21
If the decision is made to proceed with recruitment, the joint TSC and IDMC will convene again after 12 patients have completed 1 month of follow-up and for a final time decide whether to maintain, accelerate, decelerate or stop recruitment.
If the trial continues, recruitment to 21 patients will proceed at the rate determined after data from the first 12 patients has been reviewed. All participants recruited to RAFT will be followed-up for 12 months after surgery. A total of 12 months follow-up has been chosen based on research from other similar allogeneic ophthalmology trials.

In addition to convening after 6, 9, and 12 patients have sufficient follow up data to evaluate safety (and efficacy after the 9th patient), the joint TSC and IDMC will be also be consulted after

each major safety event happens (regardless of how many patients have been recruited at that point in time) and after each intermediate safety event (up to the first 6 patients only).

Study Setting
The trial will be conducted at Moorfields Eye Hospital NHS Foundation trust (MEH), London in the United Kingdom (UK). MEH is a leading provider of eye health services in the UK and is a world-class centre of excellence for ophthalmic research and education. It meets all the site eligibility criteria for the RAFT trial. No further sites are anticipated.

All trial medical assessments and procedures will be performed in an appropriate clinical setting by suitability qualified staff.

Intervention Type
Procedure/Surgery

Primary outcome measure
1. Occurrence of serious adverse events within the 12 months after surgery measured using patient records
2. Health of the surface of the cornea using a validated ocular surface scoring system at baseline and 3 months after surgery

Secondary outcome measures
1. Vision using the distance EDTRS visual acuity at 3 & 12 months after surgery
2. Quality of life using the NEI-VFQ-25 patient questionnaire and RAND 36-Item Health Survey at 3 & 12 months after surgery

Overall study start date
30/04/2019

Completion date
31/05/2025

Reason abandoned (if study stopped)
Participant recruitment issue

Eligibility

Key inclusion criteria
1. Confirmed diagnosis of congenital aniridia
2. Confirmed diagnosis of advanced aniridia related keratopathy with corneal surface conjunctivalisation, vascularisation and increasing opacity with worsening vision loss, glare & ocular surface pain
3. Patients aged 18 years and over
4. Participants must use acceptable contraception from enrolment up to 6 weeks for female participants and 90 days for male participants, after stopping immunosuppression therapy
5. Negative viral screen for, HIV, syphilis, hepatitis B & C and Human T-cell Leukaemia Virus (HTLV)
6. Negative urine pregnancy test

Participant type(s)

Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 21; UK Sample Size: 21

Total final enrolment
9

Key exclusion criteria
1. Poor tear production, as assessed by a Schirmer's test type 1
2. Lid malposition
3. Current corneal infection
4. Uncontrolled glaucoma (defined as uncontrolled eye pressure, changes to medication, recent surgery in the last 3 months or being considered for surgical treatment)
5. Must not be NPL (no light perception) in one or both eyes
6. Patients who refuse to consent to the site informing their GP of their participation
7. Patients who lack capacity to give full informed consent to participate
8. Pregnant or lactating women
9. Patients with known contraindications to any of the following non-investigational medicinal products; mycophenolate, prednisolone, omeprazole, doxycycline, dexamethasone or moxifloxacin or excipients according to the relevant SmPCs
10. Patients who are participating in any concurrent trial involving an investigational medical product, device or surgical intervention within the last 12 months
11. Known albumin or egg allergy
12. Known penicillin allergy
13. Known hydrocortisone allergy
14. Inability to lie flat for surgical procedure

Date of first enrolment
31/05/2021

Date of final enrolment
26/01/2024

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Moorfields Eye Hospital
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Sponsor information

Organisation
University College London

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Sponsor type
University/education

Website
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ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council; Grant Codes: MR/S018883/1

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

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
31/05/2026

Individual participant data (IPD) sharing plan
All data generated or analysed during this study will be included in the subsequent results publication

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No