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A study looking at a comparison between surgical procedure conceived to increase the stiffness of cornea and standard care (glasses) in children with Keratoconus

Submission date
02/11/2016

Recruitment status
No longer recruiting

Registration date
10/11/2016

Overall study status
Completed

Last Edited
21/01/2025

Condition category
Eye Diseases

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

Plain English summary of protocol

Background and study aims
Keratoconus is an eye condition in which the normally round dome-shaped clear window of the eye (cornea) becomes thinner and changes shape over time, leading to poor vision. Symptoms of keratoconus generally begin in late teenage years or early twenties but they can start at any age. If it is spotted during childhood, it is often more advanced and worsens more quickly. Patients with a suspected or confirmed diagnosis of keratoconus are usually referred to hospital clinics immediately or when they first go to get glasses. In advanced cases, a transplant surgery to replace the affected cornea is needed. Corneal collagen cross-linking (CXL) is a procedure that involves the removal of the surface layer of the cornea, the administration of riboflavin (vitamin B2) eye drops and exposure of the cornea to UV light. CXL is a new treatment that is believed to stop keratoconus from getting worse, by increasing stiffness of the cornea and stopping progression. The aim is to study the efficacy and safety of (CXL) in children with keratoconus, and to compare it to standard care with provision of glasses and/or contact lenses as required for best vision.

Who can participate?
Children aged between 10 and 16 years with mild to moderate keratoconus

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group continue to receive normal care, which involved being given glasses or contact lenses to correct their vision. Those in the second group undergo the CXL procedure. This involves having the area numbed (local anaesthetic) or being put to sleep (general anaesthetic) for the operation, in which the surface layer of the cornea is removed, vitamin B2 eye drops applied and ultraviolet light shone on the eye. Participants in both groups have their eyes examined at the start of the study and then every three months for 18 months in order to assess progression of their condition.

What are the possible benefits and risks of participating?
It is not known whether there will be any benefits involved with participating. There is a risk that some patients treated with CXL will experience pain in the treated eye 1-2 days after the procedure. There is always a risk when having surgery, most of the time these are very mild (such as feeling nauseous, tired or dizzy from the anaesthetic).

Where is the study run from?
1. Moorfields Eye Hospital (UK)
2. Royal Hallamshire Hospital (UK)
3. Royal Liverpool Hospital (UK)

When is the study starting and how long is it expected to run for?
September 2015 to December 2022 (updated 23/10/2020, previously: February 2019)

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
Dr Haripriya Tumuluri
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Study website
https://www.ucl.ac.uk/comprehensive-clinical-trials-unit/research-projects/2018/nov/keralink

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
2016-001460-11

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
32332

Study information

Scientific Title
Corneal cross-linking versus standard care in children with keratoconus, a randomised, multicentre, observer-masked trial of efficacy and safety

Acronym
KERALINK

Study objectives
The aim of KERALINK is to establish clear evidence on whether CXL is efficacious in stabilising the progression of keratoconus and safe in children and young patients between the age of 10 and 16 years.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London-Brent Research Ethics Committee, 30/06/2016, ref: 16/LO/0913

Study design
Randomised; Interventional; Design type: Treatment, Drug

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Specialty: Ophthalmology, Primary sub-specialty: Other; UKCRC code/ Disease: Eye/ Disorders of sclera, cornea, iris and ciliary body

Interventions

Participants are randomised into one of two groups in a 1:1 ratio using computer generated treatment group allocation

Intervention group: Participants receive cross-linking in one or both eyes (according to whether progression is confirmed in one eye or both eyes), under general or local anaesthesia as applicable, followed by standard management. Following removal of corneal epithelium and administration of riboflavin drops, ultraviolet light will be administered according to standardised parameters of 10mW/cm2 for a 5.4J/cm2 total energy dose.

Control group: Participants receive standard management alone, including refraction testing with provision of glasses and/or specialist contact lens fitting. Glasses or contact lenses to be provided for one or both eyes as required for best corrected visual acuity. Those patients who develop advanced disease and poor spectacle- and lens-corrected visual acuity during the course of the trial will be offered corneal transplantation.

Follow up for all participants takes place at every 3 months and involves examination of the study eye using Corneal Topography, Refraction and Corneal Ultrasound techniques.

Intervention Type
Other

Primary outcome measure
Current primary outcome measure as of 23/10/2020:
Keratoconus progression is assessed by measuring K2 by Pentacam at baseline, 18 months, and 48 months

Previous primary outcome measure as of 31/01/2019:
Keratoconus progression is assessed by measuring K2 by Pentacam at baseline and 18 months.

Previous primary outcome measure:
Keratoconus progression is assessed by measuring Kmax by Pentacam at baseline and 18 months.

Secondary outcome measures
1. Time to keratoconus progression is measured using Pentacam at baseline, post-treatment, 3, 6, 9, 12, 15 and 18 months
2. Uncorrected and best corrected visual acuity is measured using a Standard Eye Chart at baseline, post-treatment, 3, 6, 9, 12, 15 and 18 months
3. Refraction is measured using a Retinoscope at baseline, post-treatment, 3, 6, 9, 12, 15 and 18 months
4. Apical corneal thickness is measured using ultrasound at baseline, post-treatment, 3, 6, 9, 12, 15 and 18 months
5. Quality of life as assessed by using the CHU9D and CVAQC questionnaires at baseline, 6, 12 and 18 months

Overall study start date
01/09/2015

Completion date
31/12/2022

Eligibility

Key inclusion criteria
Current inclusion criteria as of 31/01/2019:
1. Age 10-16 years
2. Keratoconus progression confirmed in one or both eyes by Pentacam corneal topography. Progression will be defined as an increase of at least 1.5 dioptres in K2 or Kmax on Pentacam corneal topography.
3. Provision of informed consent and willingness to complete the patient reported outcome measures
4. Willing to attend for follow up visits

Previous inclusion criteria:
1. Age 10-16 years
2. With keratoconus progression confirmed in one or both eyes by Pentacam cornealtopography. Progression will be defined as an increase of at least 1.5 dioptres in Kmax on corneal topography between two Pentacam examinations at least 3 months apart.
3. Provision of informed consent and willingness to complete the patient reported outcome measures
4. Willing to attend for follow up visits

Participant type(s)
Patient

Age group
Child

Lower age limit
10 Years

Upper age limit
16 Years

Sex
Both

Target number of participants
Planned Sample Size: 60; UK Sample Size: 60

Total final enrolment
60

Key exclusion criteria
Current exclusion criteria as of 31/01/2019:
1. Advanced keratoconus as determined by apex corneal scarring
2. Apex corneal thickness <400 µm
3. Steepest corneal meridian (K2) >62 dioptres and maximum corneal curvature (Kmax) >70 dioptres on Pentacam topography at screening
4. Rigid contact lens wear in both eyes and unable to abstain for 7 days pre-examinations
5. Corneal comorbidity

6. Down’s syndrome
7. Any clinical condition which the investigator considers would make the patient unsuitable for the trial, including pregnancy
8. Participation in other clinical trials which would materially impact on the Keralink study

Previous exclusion criteria:
1. Advanced keratoconus as determined by apex corneal scarring
2. Apex corneal thickness 60 diopres
3. Rigid contact lens wear in both eyes and unable to abstain for 7days pre-examinations
4. Corneal co-morbidity
5. Down's syndrome
6. Any clinical condition which the investigator considers would make the patient unsuitable for the trial, including pregnancy
7. Participation in other clinical trials which would materially impact on the Keralink study

Date of first enrolment
28/10/2016

Date of final enrolment
26/09/2018

Locations

Countries of recruitment
England

United Kingdom

Wales

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

Study participating centre
Royal Hallamshire Hospital
8 Beech Hill Road
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Study participating centre

Royal Liverpool Hospital
Prescot Street
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Study participating centre
Royal Gwent Hospital
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Study participating centre
Royal Manchester Eye Hospital
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Sponsor information

Organisation
University College London

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Sponsor type
University/education

Website
http://www.ucl.ac.uk/

ROR
https://ror.org/02jx3x895

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

Results and Publications

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

Intention to publish date
31/10/2021

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study 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?
Protocol article	protocol	12/09/2019	23/10/2020	Yes	No
Statistical Analysis Plan	Statistical analysis plan	12/06/2020	23/10/2020	No	No
Results article		21/04/2021	08/12/2022	Yes	No
HRA research summary			28/06/2023	No	No
Results article		01/10/2021	21/01/2025	Yes	No