ISRCTN10524984 https://doi.org/10.1186/ISRCTN10524984

Laser for Early Age related macular Degeneration

Submission date
02/03/2013

Recruitment status
No longer recruiting

Registration date
04/06/2013

Overall study status
Completed

Last Edited
06/01/2017

Condition category
Eye Diseases

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

Plain English summary of protocol

Background and study aims
Age-related macular degeneration (AMD) affects the central part of the vision; this is the part we use for reading and seeing faces. Most people with AMD will gradually lose this vision over several years. There is no treatment although high doses of vitamins A, C and E, and the mineral zinc may help to slow it and injections of a drug into the eye may help a minority of patients who develop abnormal blood vessels associated with the AMD.
The purpose of this study is to find out whether using a newly developed laser on the back of the eye can safely improve or stabilise eyesight in patients who have signs of intermediate to high-risk Early AMD. The Ellex 2RT laser is capable of delivering very short pulses of laser that selectively target pigment granules in the layer of cells that supports the light-sensitive retina. Stimulating this layer with short pulses of laser has been shown to result in the disappearance of waste material from beneath it that is the characteristic of AMD.

Who can participate?
The study aims to recruit 40 people with early AMD. They will have a risk of developing visual loss as a result of AMD of 12-50% within 5 years in the study eye.

What does the study involve?
To test the effectiveness of 2RT in the treatment of with intermediate to high-risk Early AMD we will divide participants into two groups at random half will receive treatment with 2RT laser and half will be exposed to a completely harmless flash of light. We will perform detailed tests of subjects vision before doing this some of these tests are routinely performed in eye clinics (for example reading an eye chart) others may require subjects to press a button when they see a light (a field test) or to have a scan of the back of the eye. None of these tests involve touching the eye.
On the day of the intervention those receiving the laser will have it applied to 12 areas just outside the macula (the part of the eye responsible for central vision)of the eye in which they have the worst vision. This involves putting a drop which dilates the pupil and a drop of some anaesthetic into the eye. A special hand-held contact lens will be applied to the eye to help focus the laser. This process takes about 20 minutes and whilst they may see some flashes of light they should not feel anything except some pressure from the contact lens on the eye.
A week after the laser has been applied subjects will be asked to come back for some repeats of

the tests they had at the start of the trial. We will then ask them to come back at 6 weeks after the laser was applied, at 3 months and at 1 year.

What are the possible benefits and risks of participating?
It has been known for many years that applying conventional laser to the back of the eye in patients with Early AMD can cause the disappearance of waste products (known as drusen) from under the light-sensitive retina. It is not known whether triggering the disappearance of drusen is associated with any visual benefit but there are theoretical reasons why this may be so. The laser probably drives the disappearance of drusen by causing a small amount of inflammation when it damages the cell layer under the retina. Unfortunately it can be difficult to control the amount of damage conventional lasers can cause. This trial is designed to test the safety and effectiveness of a new type of laser that is much gentler and causes less damage than those lasers available more widely. Results of a recent trial in Australia suggest that the laser we will be testing in this trial is capable of improving vision in patients with high-risk Early AMD.
All laser surgical procedures carry a risk of side effects. We believe the risks of immediate side effects to be much lower with this new type of laser but cannot rule them out completely.
If too much laser is applied it can damage the overlying retina and cause a permanent black spot in visual field. We will be applying the laser outside of the part of the retina responsible for central vision but there is a theoretical risk that the laser could strike the centre of the macula and permanently affect a participants ability to read or see faces clearly. If this occurred they would still retain their peripheral vision (outer vision), which means it will not cause complete blindness.
Aggressive laser treatment can also cause blood vessels to grow underneath the retina in the treated area again causing distortion or a permanent black spot in the vision. The risks of this are very low and if it occurs the blood vessels usually disappear on their own.
The results of other trials investigating the use of this new laser in the treatment of diabetic macular disease suggest that it is at least as effective and safe as standard laser.
In the long term there is not enough evidence to say for certain whether the new laser we will be applying does not make AMD worse. There is limited evidence to suggest that much more damaging conventional laser does not cause worsening of vision even 8 years after its application in this context.

Where is the study run from?
The study is being conducted by the London Eye Hospital, a private eye hospital located on Wimpole St and Harley St in London.

When is the study starting and how long is it expected to run for?
The study is starting in June 2013 and is expected to last 18 months.

Who is funding the study?
The study is funded by London Eye Hospital Ltd

Who is the main contact?
Mr M A Qureshi, Medical Director of the London Eye Hospital and Chief Investigator for the study
London Eye Hospital
29a Wimpole Street
London
W1G 8PG
United Kingdom

Contact information

Type(s)
Scientific

Contact name
Mr Muhammad Qureshi

Contact details
London Eye Hospital
29a Wimpole Street
London
United Kingdom
W1G 8PG

Additional identifiers

Protocol serial number
LEH0001

Study information

Scientific Title
A randomised controlled trial of the use of LR1532 Ellex 2RT in the treatment of early age related macular degeneration (AMD)

Acronym
LEAD

Study objectives
Nanopulse laser to the posterior pole stimulates the resorption of drusen in intermediate to high-risk early AMD and this is associated with an improvement in macular function.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London Eye Hospital ethical board, November 2012, ref: LEH 0001

Study design
Single-centre interventional randomised single-blind placebo-controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Age related macular degeneration

Interventions
Training on the Ellex 2RTTM will be provided by Ellex Australia and Ellex Services Europe in advance of the trial start date.

Set-up: The patient will have local anaesthetic drops and guttae tropicamide 1% instilled in the conjunctival sac of the eye to be treated. After 15 minutes the patients head will be positioned on the chin-rest of the 2RT laser system and the slit-lamp microscope positioned to observe the eye selected for intervention.

At this stage patients scheduled to receive placebo will be exposed to the bright white light flash delivered by the 2RTTM

Patients scheduled to receive nanopulse laser will be managed as follows:
1. Contact lens: Area Centralis 1:1 laser contact lens (or equiv) to be used for viewing and laser application. Apply this to the eye for intervention.
2. Energy setting: Apply test shots of repeated single laser pulses spaced approximately one laser spot diameter (400micron) apart outside the arcades while increasing the energy until a faintly visible blanching of the lasered spot is observed. The starting energy should be set to 0.14 mJ and increased by 2 steps until the blanching point is reached using no more than 12 laser shots. Energy is not to be increased beyond 0.4mJ.
3. Illumination should be set to a low level to provide good contrast viewing of blanching.
4. Reduce the energy by one steps of this setting and then apply in the outer macula as described below in point 5
5. Spot placement: 12 laser shots in two arcs of 6 shots superior and 6 shots inferior, inside the retinal vascular arcades at an approximate distance from the fovea of 3000 um, with approximately one laser spot diameter between them.
6. Particular attention should be paid to any signs of bleeding within the laser spot area. If this occurs apply slight pressure with the contact lens until it stops and do not apply further test shots. Reduce the laser energy by 2 steps in this case and apply in the outer macula.

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
1. Loss of <10 Early Treatment Diabetic Retinopathy Study (ETDRS) letters
2. ETDRS best corrected visual acuity in the intervention eye at 3 months (based on published coefficient of repeatability 95% for ETDRS acuity in intermediate to high-risk Early AMD)

Key secondary outcome(s)
Significant ($p<0.05$) improvement in sensitivity in 3 or more test areas on MaiaTM microperimetry testing at 3 months.

Completion date
01/04/2014

Eligibility

Key inclusion criteria

1. Age-Related Eye Disease Study (AREDS) simplified severity scale for AMD score of 2 or more
2. Bilateral drusen >125µm and pigmentary abnormalities (AREDS simplified severity risk score 4)
3. Pigmentary abnormalities in both eyes (AREDS simplified severity risk score 2)
4. Intermediate drusen (63 µm) in both eyes and at least one eye with pigment abnormalities (AREDS simplified severity risk score 2)
5. A combination of pigment abnormalities and large drusen >125µm (either eye; AREDS simplified severity risk score 2)
6. At least one eye with neovascular AMD (AREDS simplified severity risk score 2)
7. At least one eye with geographic atrophy (GA)
8. Male and female, age>50

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Ocular disease in either eye, other than AMD, that compromises the ability to treat or visualize the fundus or would compromise the ability to assess any effect following laser application, including:
1.1. Diabetic retinopathy unless retinopathy is limited to fewer than 10 microaneurysms and/or small retinal haemorrhages and without thickening on optical coherence tomography (OCT)
1.2. Uncontrolled glaucoma; a significant glaucomatous change (optic cup-disc ratio >0.7; intraocular pressure (IOP) >26mmHg on 2 or more occasions in at least one eye) ocular anti-hypertensive treatment is permitted as long as IOP is well-controlled with no field loss encroaching onto the macula
1.3. Other retinal diseases such as angioid streaks, central serous retinopathy
1.4. Epiretinal membrane of significant size located in the macular area
1.5. Optic atrophy
1.6. Pigmentary abnormalities used to qualify for inclusion that are not typical of AMD (such as myopia, pattern dystrophy or central serous retinopathy
1.7. Moderate myopia (5D) where the fundus presents as a typical myopic fundus with a myopic crescent at the disc with width ≥50% of the longest diameter of the disc.
1.8. Macular hole or pseudohole
1.9. Retinal vein occlusion, active uveitis, presumed ocular histoplasmosis syndrome, other sight-threatening retinopathies and retinal degeneration. Significant explained or unexplained visual loss.
1.10. A choroidal naevus within 2 DD of the centre of the macula associated with depigmentation or overlying atypical drusen
2. Other ocular diseases or conditions, the presence of which may now or in the future complicate evaluation of AMD
Amblyopia (mild amblyopia without significant VA loss can be included)
3. Chronic requirement for any systemic or ocular medication administered for other diseases and known to be toxic to the retina or optic nerve, such as:

3.1. Desferioxamine
3.2. Chloroquine/hydroxycholoroquine
3.3. Chorpromazine
3.4. Phenothiazines
3.5. Chronic systemic steroid use of at least 10mg per day or more
3.6. Ethambutol
4. Significant cataract
5. Nuclear cataract grade 2 or 3; cortical cataract grade 2 or 3; posterior subcapsular cataract grade 2 or 3 (using simplified cataract grading system for international epidemiological studies

Date of first enrolment
01/04/2013

Date of final enrolment
01/04/2014

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
London Eye Hospital
London
United Kingdom
W1G 8PG

Sponsor information

Organisation
London Eye Hospital (UK)

ROR
https://ror.org/01spx4y35

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
London Eye Hospital (UK)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration