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StereoTactic radiotherapy for wet Age-Related macular degeneration (STAR)

Submission date 28/11/2014	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol
Registration date 13/12/2014	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 01/11/2023	**Condition category** Eye Diseases	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims

Age-related macular degeneration (AMD) is a painless eye condition that leads to loss of central vision. There are two main types of AMD, called dry AMD and wet AMD. Wet AMD is more serious and without treatment, vision can deteriorate within days. This study investigates the use of radiation to treat wet AMD, called stereotactic radiosurgery. The radiation is delivered using a robotically controlled device that projects overlapping beams of radiation onto the macula, the part of the eye that is affected by wet AMD. This study aims to determine if stereotactic radiosurgery can maintain vision and reduce the need for regular injections of ranibizumab (the standard anti-VEGF drug used to treat wet AMD).

Who can participate?:

Males and females aged 50 years or over with wet AMD requiring anti-VEGF treatment at the time of entry to the study.

What does the study involve?

Participants will be randomly allocated to receive either radiation (stereotactic radiotherapy) or simulated placebo (sham) treatment. They will be followed up regularly for two years, and then again at the end of three and four years for a safety visit. Participants will also receive injections of ranibizumab (Lucentis) into their eye if their wet AMD is active.

What are the possible benefits and risks of participating?

The main benefit of stereotactic radiotherapy is that it may reduce the number of eye injections that people require, or in some cases eliminate them entirely. Previous studies have suggested that the patients who will be eligible for the study would obtain a better vision outcome with radiotherapy (with injections as needed) than with injections alone. The main risk of radiation is that it can sometimes damage the healthy tissue in the macula and thereby damage vision. Subtle changes to the macula can sometimes be seen using specialised testing (fluorescein angiography) but in the majority of people this does not affect the vision.

Where is the study run from?

King's College Hospital (UK).

When is the study starting and how long is it expected to run for?
Recruitment to the study will begin in December 2014 and continue for approximately 41 months. Each participant will be in the study for 4 years.

Who is funding the study?
NIHR Efficacy and Mechanism Evaluation Programme (UK).

Who is the main contact?
Mr Tim Jackson
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Study website
www.starstudy.org.uk

Contact information

Type(s)
Scientific

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Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
86810

ClinicalTrials.gov number
NCT02243878

Secondary identifying numbers
IRAS 86810

Study information

Scientific Title
StereoTactic radiotherapy for wet Age-Related macular degeneration (STAR): a randomised, double-masked, sham-controlled, clinical trial comparing low-voltage X-ray irradiation with as needed ranibizumab to as needed ranibizumab monotherapy

Acronym
STAR

Study objectives
The study's primary hypothesis is that the mean number of ranibizumab injections during the first 24 months after randomization will be less in the SRT group than in the sham group. The secondary hypothesis is that participants who undergo SRT will have a non-inferior visual outcome compared with those in the sham group.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee London - City & East, REC ref: 13/LO/1207

Study design
Randomised double-masked sham-controlled pivotal clinical trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

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
Retinal disease/age-related macular degeneration

Interventions
Participants in the treatment arm will receive 16 Gray stereotactic radiotherapy (SRT) with a concomitant injection of ranibizumab.

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Not provided at time of registration

Primary outcome measure
The primary outcome is the mean number of ranibizumab injections over 24 months. SRT will be considered superior to sham if the mean number of injections in the SRT group is statistically less than (one-sided $p<0.025$) the mean in the sham group.

Secondary outcome measures
SRT will be considered non-inferior to sham treatment if the lower bound of the 95% confidence interval for the difference in mean change in ETDRS VA at 24 months, between the SRT and sham groups, is no greater than 5 letters.

Overall study start date
01/12/2014

Completion date
30/06/2024

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 01/08/2018:
1. Participants must have neovascular AMD in the study eye, for which they have received at least three prior intravitreal injections of either bevacizumab (Avastin), aflibercept (Eylea), ranibizumab (Lucentis) or pegaptanib (Macugen)
2. Participants must have received an anti-VEGF injection in the study eye within 3 months prior to enrolment
3. Participants must require treatment with anti-VEGF therapy at the time of enrolment, due to OCT evidence of subretinal fluid and/or cystoid macular oedema, and have a macular volume that is greater than a pre-defined threshold that varies for each different make of SD-OCT

machine
4. Participants must be at least 50 years of age

Previous participant inclusion criteria:
1. Participants must have neovascular AMD in the study eye, for which they have received at least three prior intravitreal injections of either bevacizumab (Avastin), aflibercept (Eylea), ranibizumab (Lucentis) or pegaptanib (Macugen)
2. Participants must have received an anti-VEGF injection in the study eye within 3 months prior to enrolment
3. Participants must require treatment with anti-VEGF therapy at the time of enrolment, due to OCT evidence of subretinal fluid and/or cystoid macular oedema, and a macular volume that is greater than the 95th percentile of normal for the SD-OCT machines used in the investigational sites
4. Participants must be at least 50 years of age

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
411

Total final enrolment
411

Key exclusion criteria
Current participant exclusion criteria as of 01/08/2018:
1. Disciform scarring that involves the fovea, in the study eye
2. Visual acuity worse than 6/96 (24 ETDRS letters) in the study eye
3. Lesion size greater than 4 mm in greatest linear dimension, or greater than 2 mm from the centre of the fovea to the furthest point on the lesion perimeter
4. An axial length of less than 20 mm, or greater than 26 mm, in the study eye
5. Contraindication or sensitivity to contact lens application, including recurrent corneal erosions, in the study eye
6. Type 1 or Type 2 diabetes mellitus
7. Retinopathy in the study eye
8. Prior or current therapies in the study eye for age-related macular degeneration, other than anti-VEGF agents, including submacular surgery, subfoveal thermal laser photocoagulation, photodynamic therapy (PDT), or transpupillary thermotherapy (TTT)
9. Presence of an intravitreal device in the study eye
10. Previous radiation therapy to the study eye, head or neck with the exception of radio-iodine treatment for hyperthyroidism, epimacular brachytherapy to the non-study eye, or Oraya SRT to the non-study eye

11. Inadequate pupillary dilation or significant media opacities in the study eye, including cataract, which may interfere with visual acuity testing, the clinical evaluation of the posterior segment, or fundus imaging
12. Study eyes with CNV due to causes other than AMD, including presumed ocular histoplasmosis syndrome (POH), angioid streaks, multifocal choroiditis, choroidal rupture, and pathological myopia (greater than 8 Dioptres spherical equivalent). Participants with retinal angiomatous proliferation (RAP) or idiopathic polypoidal choroidal vasculopathy (IPCV) are not excluded
13. Known allergy to intravenous fluorescein, ICG or intravitreal ranibizumab
14. Intraocular surgery or laser-assisted in situ keratomileusis (LASIK) in the study eye within 12 weeks prior to enrolment
15. Prior pars plana vitrectomy in the study eye
16. Current participation in another interventional clinical trial, or participation in such a clinical trial within the last six months
17. Unwilling, unable, or unlikely to return for scheduled follow-up for the duration of the trial
18. Women who are pregnant at the time of radiotherapy
19. Participants with an implantable cardioverter defibrillator (ICD) or pacemaker implant (or any implanted device) where the device labelling specifically contraindicates patients undergoing X-ray
20. Any other condition, which in the judgment of the investigator, would prevent the participant from granting informed consent or completing the study, such as dementia and mental illness (including generalized anxiety disorder and claustrophobia)

Previous participant exclusion criteria:
1. Disciform scarring that involves the fovea, in the study eye
2. Geographic atrophy that involves the fovea, or an area of geographic atrophy that is more than 500 microns in greatest diameter, immediately adjacent to the fovea, in the study eye
3. Visual acuity worse than 6/96 (24 ETDRS letters) in the study eye
4. Lesion size greater than 4 mm in greatest linear dimension, or greater than 2 mm from the centre of the fovea to the furthest point on the lesion perimeter
5. Distance from the center of the fovea to the nearest edge of the optic disc less than 3 mm in the study eye (this distance is confirmed by the Oraya SRT device software immediately prior to treatment)
6. An axial length of less than 20 mm, or greater than 26 mm, in the study eye
7. Contraindication or sensitivity to contact lens application, including recurrent corneal erosions, in the study eye
8. Type 1 or Type 2 diabetes mellitus
9. Retinopathy in the study eye
10. Prior or current therapies in the study eye for age-related macular degeneration, other than anti-VEGF agents, including submacular surgery, subfoveal thermal laser photocoagulation, photodynamic therapy (PDT), or transpupillary thermotherapy (TTT)
11. Presence of an intravitreal device in the study eye
12. Previous radiation therapy to the study eye, head or neck with the exception of radio-iodine treatment for hyperthyroidism, epimacular brachytherapy to the non-study eye, or Oraya SRT to the non-study eye
13. Inadequate pupillary dilation or significant media opacities in the study eye, including cataract, which may interfere with visual acuity testing, the clinical evaluation of the posterior segment, or fundus imaging
14. Likely to need cataract surgery in the study eye within two years of enrolment
15. Study eyes with CNV due to causes other than AMD, including presumed ocular histoplasmosis syndrome (POH), angioid streaks, multifocal choroiditis, choroidal rupture, and pathological myopia (greater than 8 Dioptres spherical equivalent). Participants with retinal

angiomatous proliferation (RAP) or idiopathic polypoidal choroidal vasculopathy (IPCV) are not excluded
16. Known allergy to intravenous fluorescein, ICG or intravitreal ranibizumab
17. Intraocular surgery or laser-assisted in situ keratomileusis (LASIK) in the study eye within 12 weeks prior to enrolment
18. Prior pars plana vitrectomy in the study eye
19. Current participation in another interventional clinical trial, or participation in such a clinical trial within the last six months
20. Unwilling, unable, or unlikely to return for scheduled follow-up for the duration of the trial
21. Women who are pregnant at the time of radiotherapy
22. Participants with an implantable cardioverter defibrillator (ICD) or pacemaker implant (or any implanted device) where the device labelling specifically contraindicates patients undergoing X-ray
23. Any other condition, which in the judgment of the investigator, would prevent the participant from granting informed consent or completing the study, such as dementia and mental illness (including generalized anxiety disorder and claustrophobia)

Date of first enrolment
01/12/2014

Date of final enrolment
31/12/2019

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
King's College Hospital
Ophthalmology Department
Normanby Building
Denmark Hill
London
United Kingdom
SE5 9RS

Study participating centre
University Hospitals Bristol NHS Trust
Bristol Eye Hospital
Lower Maudlin Street
Bristol
United Kingdom
BS1 2LX

Study participating centre
Frimley Park Hospital
Frimley Park Hospital
Portsmouth Road
Frimley
Camberley
United Kingdom
GU16 7UJ

Study participating centre
Maidstone and Tunbridge Wells NHS Trust
The Maidstone Hospital
Hermitage Lane
Maidstone
United Kingdom
ME16 9QQ

Study participating centre
The Royal Wolverhampton NHS Trust
New Cross Hospital
Wolverhampton Road
Heath Town
Wolverhampton
United Kingdom
WV10 0QP

Study participating centre
East Lancashire Hospitals NHS Trust
Royal Blackburn Hospital
Haslingden Road
Blackburn
United Kingdom
BB2 3HH

Study participating centre
The Sussex Eye Hospital
Eastern Road
Brighton
United Kingdom
BN2 5BF

Study participating centre
William Harvey Hospital
Kennington Road
Willesborough
Ashford
United Kingdom
TN24 0LZ

Study participating centre
Hillingdon Hospital
Hillingdon Hospital
Pield Heath Road
Uxbridge
United Kingdom
UB8 3NN

Study participating centre
Whipps Cross University Hospital NHS Trust
Whipps Cross Hospital
Whipps Cross Road
London
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E11 1NR

Study participating centre
Princess Alexandra Hospital
Hamstel Road
Harlow
United Kingdom
CM20 1QX

Study participating centre
Norfolk and Norwich University Hospitals NHS Foundation Trust
Colney Lane
Colney
Norwich
United Kingdom
NR4 7UY

Study participating centre

Essex County Hospital
Lexden Road
Colchester
United Kingdom
CO3 3NB

Study participating centre
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The Calderdale Royal Hospital
Huddersfield Road
Halifax
United Kingdom
HX3 0PW

Study participating centre
Stoke Mandeville Hospital
Mandeville Road
Aylesbury
United Kingdom
HP21 8AL

Study participating centre
James Paget University Hospitals NHS Foundation Trust
Lowestoft Road
Gorleston
Great Yarmouth
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NR31 6LA

Study participating centre
Royal Derby Hospital
Uttoxeter Road
Derby
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DE22 3NE

Study participating centre
Queens Hospital
Rom Valley Way

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RM7 0AG

Study participating centre
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Bordesley Green
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B9 5SS

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Acton Lane
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Study participating centre
Salisbury District Hospital
Odstock Road
Salisbury
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SP2 8BJ

Study participating centre
Cambridge University Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
St Helier Hospital
Wrythe Lane
Carshalton
United Kingdom
SM5 1AA

Study participating centre
Lincoln County Hospital
Greetwell Road
Lincoln
United Kingdom
LN2 5QY

Study participating centre
Leighton Hospital
Leighton
Crewe
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CW1 4QJ

Study participating centre
Yeovil District Hospital
Higher Kingston
Yeovil
United Kingdom
BA21 4AT

Study participating centre
Dorset County Hospital
Williams Avenue
Dorchester
United Kingdom
DT1 2JY

Study participating centre
Hinchingbrooke Hospital
Hinchingbrooke Park
Huntingdon
United Kingdom
PE29 6NT

Sponsor information

Organisation

King's College Hospital NHS Foundation Trust

Sponsor details
King’s College Hospital
Denmark Hill
London
England
United Kingdom
SE5 9RS

Sponsor type
Hospital/treatment centre

Website
https://www.kch.nhs.uk/research

ROR
https://ror.org/01n0k5m85

Organisation
King's College London

Sponsor details
Strand Campus
The Strand
London
England
United Kingdom
WC2R 2LS

Sponsor type
University/education

Website
http://www.kcl.ac.uk/index.aspx

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
30/06/2025

Individual participant data (IPD) sharing plan
The 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?
Protocol article	protocol	24/11/2016		Yes	No
HRA research summary			28/06/2023	No	No
Protocol file	version 1.9	25/01/2019	01/11/2023	No	No