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Clinical efficacy and mechanistic evaluation of Eplerenone for central serous chorio-retinopathy – the VICI randomised trial

Submission date 04/05/2016	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 06/05/2016	**Overall study status** Completed	
Last Edited 08/07/2025	**Condition category** Eye Diseases	

Plain English summary of protocol

Background and study aims
Central serous chorio-retinopathy (CSCR) is a poorly understood eye disease involving the retina. The retina is a layer of light-sensitive cells at the back of the eye which are responsible for converting light into electrical signals that are carried to the brain, where they are interpreted as the images we see. In CSCR, fluid (which leaks from a layer of tissue underneath the retina called the choroid) builds up under the retina causing vision to become distorted and leading to vision loss in around a third of cases. The exact cause of CSCR is unknown however there does appear to be a genetic link, as it often appears in members of the same family. Currently, there are no proven effective treatments. Recently a few patients have responded to treatment with a drug called eplerenone, which removes the fluid buildup and improves vision. However, information on the long term benefit and safety of this drug is lacking. The aim of this study is to test the effectiveness of eplerenone in the treatment of CSCR.

Who can participate?
Adults with visual impairment due to central serous chorio-retinopathy (CSCR)

What does the study involve?
Participants are randomly allocated to be treated with either a capsule containing eplerenone or a placebo capsule containing no active ingredients. For patients in the eplerenone group, a dosage of 25 mg per day is given, which can be increased to 50mg after one week if tolerated. Participants attend study visits at four weeks and then three, six, nine and twelve months. At each visit, participants undergo sight tests, an eye examination, completing a number of questionnaires, as well as having blood samples taken. Participants are also asked for permission to take an additional blood sample at their first visit, so that the genetic material and other components from their blood can be stored for a future study. If the CSCR has resolved at any of these visits, the treatment is stopped (it can be restarted if it reoccurs).

What are the possible benefits and risks of participating?
There is no guarantee that the treatment used in this study will help individual participants, however the information from the results could help patients in the future. There are side

effects associated with eplerenone usage but these will be managed through regular patient and safety data monitoring. There is also a small risk of pain or bruising during and after blood tests.

Where is the study run from?
Twenty hospitals in England and Ireland (UK)

When is the study starting and how long is it expected to run for?
January 2016 to April 2019

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

Who is the main contact?
Prof. Andrew Lotery
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Contact information

Type(s)
Public

Contact name
Prof Andrew Lotery

Contact details
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Additional identifiers

Clinical Trials Information System (CTIS)
2016-000113-70

Protocol serial number
20848

Study information

Scientific Title

Clinical efficacy and mechanistic evaluation of Eplerenone for central serous chorio-retinopathy – the VICI randomised trial

Acronym
VICI

Study objectives
The aim of the study is to compare the efficacy and safety of eplerenone with usual care versus placebo with usual care in the treatment of chronic Central serous chorio-retinopathy (CSCR).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Wales Research Ethics Committee 1, 30/04/2016, ref: 16/WA/0069
Amendment 1 received 04/07/2016; Amendment 2 received 15/11/2016; Amendment 3 received 06/02/2017; Amendment 4 received 23/03/2017; Amendment 5 received 13/04/2017; Amendment 6 approved 22/03/2018.

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

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Specialty: Ophthalmology, Primary sub-specialty: Glaucoma; UKCRC code/ Disease: Eye/ Disorders of choroid and retina

Interventions
Patients who consent will be randomised using an online system to active drug (Eplerenone) or placebo. They will be given a 25-mg dose (tablet form) for 1 week, reviewed and if tolerated the dose will be increased to 50 mg. They will be reviewed again at 4 weeks and then every 3 months for a year. Their vision will be assessed using visual acuity (letter charts) and specialised ophthalmic imaging, as well as quality of life questionnaires at the start and the end of the study. Treatment will be stopped at week 4, months 3, 6, 9 or 12 if there is complete resolution of sub-retinal fluid (SRF) under the fovea in the study eye. Treatment will be restarted at a subsequent visit if there is recurrence of sub-foveal SRF. The same dose escalation process will apply on restarting treatment. Treatment will be stopped for individual patients if they develop a complication of taking eplerenone. Also if at any of study visits visual acuity drops by 15 or more letters, the ophthalmologist may consider alternative therapies and may decide to stop the study intervention.

Intervention Type
Other

Phase
Phase III

Primary outcome(s)

Primary outcome as of 23/01/2017:
Best Corrected Visual Acuity measured using validated ETDRS vision charts, at the 12 month visit, adjusted for baseline BCVA.

Original primary outcome:
The change in Best Corrected Visual Acuity measured using validated ETDRS vision testing at baseline, 4 weeks, 3, 6, 9 and 12 months.

Key secondary outcome(s))

Current secondary outcomes as of 05/03/2019:
1. Low luminance BCVA. This is measured immediately after measuring BCVA by adding a 2 log neutral density filter and recording the number of letters read.
2. CSRT as measured by OCT recorded at 12 months, including CSRT measured at interim visits and adjusted for baseline CSRT.
3. Change in sub-retinal fluid thickness as measured by OCT
4. Systemic and ocular adverse events at any time during the 12 month follow-up period
5. Proportion of patients with macular atrophy of the RPE defined as hypoautofluorescence at 12 months
6. Area change in macular RPE hypoautofluorescence at 12 months.
7. Choroidal thickness as measured by enhanced depth imaging OCT at 12 months, adjusted for baseline choroidal thickness. Measurements to be made sub-foveally.
8. Proportion of patients with reduced choroidal permeability on ICG at 12 months
9. Time to resolution of SRF.
10. Classification of all study eyes as complete, partial or no resolution of SRF at each time point of the study. Partial resolution of SRF is defined as a decrease of >25 % of CMT from baseline. A non-responder is defined as having an increase in SRF or decrease in SRF ≤25% from baseline.
11. Patient-reported visual function using Visual Function Questionnaire VFQ 25 will be assessed at baseline and 12 months.
12. Classification of all study eyes by each FFA phenotype, such as smoke stack, ink-blot and chronic epitheliopathy at baseline and 12 months.
13. Classification of all study eyes as early, late, or non responder. An early responder is defined as complete or partial resolution of sub-foveal SRF by 3 months. A late responder is defined as complete or partial resolution of sub-foveal SRF after 6 months.
14. Incidence of CSCR in the fellow eye as measured by OCT, FFA, ICGA or AF.
15. Time to recurrence of SRF. Recurrence will be defined as the appearance of new SRF in a study eye after complete resolution of SRF at any point.

Previous secondary outcomes as of 05/03/2019:
1. Low luminance BCVA. This is measured immediately after measuring BCVA by adding a 2 log neutral density filter and recording the number of letters read.
2. CSRT as measured by OCT recorded at 12 months, including CSRT measured at interim visits and adjusted for baseline CSRT.
3. Change in sub-retinal fluid thickness as measured by OCT
4. Systemic and ocular adverse events at any time during the 12 month follow-up period
5. Proportion of patients with macular atrophy of the RPE defined as hypoautofluorescence at 12 months
6. Area change in macular RPE hypoautofluorescence at 12 months.
7. Choroidal thickness as measured by enhanced depth imaging OCT at 12 months, adjusted for baseline choroidal thickness. Measurements to be made sub-foveally.
8. Proportion of patients with reduced choroidal permeability on ICG at 12 months

9. Time to resolution of SRF.
10. Classification of all study eyes as complete, partial or no resolution of SRF at each time point of the study. Partial resolution of SRF is defined as a decrease of >25 % of CMT from baseline due to resolution of SRF. A non-responder is defined as having an increase in SRF or decrease in SRF ≤25% from baseline. Recurrence will be defined as the appearance of new SRF in a study eye after complete resolution of SRF at any point.
11. Patient-reported visual function using Visual Function Questionnaire VFQ 25 will be assessed at baseline and 12 months.
12. Classification of all study eyes by each FFA phenotype, such as smoke stack, ink-blot and chronic epitheliopathy
13. Classification of all study eyes as early, late, or non responder. An early responder is defined as complete or partial resolution of sub-foveal SRF by 3 months. A late responder is defined as complete or partial resolution of sub-foveal SRF after 6 months.
14. Incidence of CSCR in the fellow eye as measured by OCT, FFA, ICGA or AF.

Previous secondary outcomes as of 12/01/2017:
1. Low luminance visual acuity is measured immediately after measuring BCVA at baseline, 4 weeks, 3, 6, 9 and 12 months by adding a 2 log neutral density filter and recording the number of letters read
2. Central subfield retinal thickness (CSRT) as measured by optical coherence tomography (OCT) estimated at 12 months, including CSRT measured at interim visits and adjusted for baseline CSRT
3. Change in sub-retinal fluid (SRF)thickness as measured by OCT at 12 months
4. Systemic and ocular adverse events at any time during the 12 month follow-up period
5. Proportion of patients with macular atrophy of the Retinal pigment epithelium (RPE) defined as hypoautofluorescence at 12 months
6. Area change in macular RPE hypoautofluorescence at 12 months
7. Choroidal thickness as measured by enhanced depth imaging OCT at 12 months, adjusted for baseline choroidal thickness
8. Proportion of patients with reduced choroidal permeability on Indocyanine green angiography at 12 months
9. Time to resolution of SRF as measured by OCT at 4 weeks, 3, 6, 9 and 12 months
10. Proportion of patients with complete resolution of SRF at each time point of the study
11. Patient-reported visual function using Visual Function Questionnaire VFQ 25 will be assessed at baseline and 12 months
12. Classification of all study eyes as complete, partial or no resolution of SRF at each time point of the study. Partial resolution of SRF is defined as a decrease of >25 % of CMT from baseline due to resolution of SRF. A non-responder is defined as having an increase in SRF or decrease in SRF ≤25% from baseline. Recurrence will be defined as the appearance of new SRF in a study eye after complete resolution of SRF at any point.
13. Classification of all study eyes by each FFA phenotype, such as smoke stack, ink-blot and chronic epitheliopathy, is assessed at baseline
14. Classification of all study eyes as early, late, or non responder. An early responder is defined as complete or partial resolution of sub-foveal SRF by 3 months. A late responder is defined as complete or partial resolution of sub-foveal SRF after 6 months
15. Incidence of CSCR in the fellow eye as measured by OCT, FFA, ICGA or AF at baseline, 4 weeks, 3, 6, 9 and 12 months

Original secondary outcomes:
1. Low luminance visual acuity is measured immediately after measuring BCVA at baseline, 4 weeks, 3, 6, 9 and 12 months by adding a 2 log neutral density filter and recording the number of letters read

2. Central subfield retinal thickness (CSRT) as measured by optical coherence tomography (OCT) estimated at 12 months, including CSRT measured at interim visits and adjusted for baseline CSRT
3. Change in sub-retinal fluid (SRF) volume as measured by OCT at 12 months
4. Systemic and ocular adverse events at any time during the 12 month follow-up period
5. Proportion of patients with macular atrophy of the Retinal pigment epithelium (RPE) defined as hypoautofluorescence at 12 months
6. Area change in macular RPE hypoautofluorescence at 12 months
7. Choroidal thickness as measured by enhanced depth imaging OCT at 12 months, adjusted for baseline choroidal thickness
8. Proportion of patients with reduced choroidal permeability on Indocyanine green angiography at 12 months
9. Time to resolution of SRF as measured by OCT at 4 weeks, 3, 6, 9 and 12 months
10. Proportion of patients with complete resolution of SRF at each time point of the study
11. Patient-reported visual function using Visual Function Questionnaire VFQ 25 will be assessed at baseline and 12 months
12. Correlation of final visual acuity (12 months) with age of patient
13. Correlation of presence of granular/confluent hypoautofluorescence in macula with final visual acuity at 12 months
14. Proportion of each Fundus Fluorescein angiogram phenotype such as smoke stack, ink-blot and chronic epitheliopathy at 12 months

Completion date
31/07/2019

Eligibility

Key inclusion criteria
Inclusion criteria as of 12/01/2017:
1. Aged between 18 and 60 years
2. Visual impairment due to CSCR of ≥ 4 months duration defined as:
2.1. Subfoveal presence of SRF on OCT
AND
2.2. Characteristic appearance of CSCR on FFA and Indocyanine-green angiography (ICGA).
AND
2.3. Investigator believes that there is sufficient evidence from patient history, case note documentation or appearance of the macula that CSCR has been present for at least 4 months
3. Women must be willing to use effective contraception, be surgically sterile or post-menopausal for >12 months
4. Able to provide written informed consent

The following additional inclusions apply to a study eye only (i.e. they may be present for a non-study eye):
1. A study eye should have an Early Treatment Diabetic Retinopathy Study (ETDRS) BCVA score greater than 53 letters and less than 86 letters
2. A study eye should have clear ocular media and adequate pupillary dilatation to permit photography

It is rare but not impossible for patients to present with CSCR in both eyes or CSCR may develop in the fellow eye during the trial. We propose to measure eye-specific outcomes such as BCVA in both eyes throughout the trial, designating eyes as study eyes or not. Statistical analyses will

take into account the availability of data for two eligible eyes in one patient. If both eyes present with CSCR at baseline, the clinical trial site will decide which is the primary eye and this eye will have retinal imaging performed first. The primary eye would usually be the one with most active disease/most subretinal fluid. It will be identified by OCT imaging and subsequent investigations such as fluorescein and indocyanine green angiography will then be performed initially on this eye. If a patient presents with one affected eye and the fellow eye subsequently develops CSCR the eye first affected will always be the primary study eye.

Original inclusion criteria:
1. Aged between 18 and 60 years
2. Visual impairment due to central serous chorio-retinopathy (CSCR) of ≥ 4 months duration defined as:
2.1. Subfoveal presence of sub-retinal fluid (SRF) on OCT
AND
2.2. Characteristic appearance of CSCR on FFA and Indocyanine-green angiography (ICGA).
3. Women must be willing to use effective contraception, be surgically sterile or post-menopausal for >12 months
4. Able to provide written informed consent

The following additional inclusions apply to a study eye only (i.e. they may be present for a non-study eye):
5. A study eye should have an Early Treatment Diabetic Retinopathy Study (ETDRS) BCVA score greater than 53 letters and less than 79 letters
6. A study eye should have clear ocular media and adequate pupillary dilatation to permit photography

It is rare but not impossible for patients to present with CSCR in both eyes or CSCR may develop in the fellow eye during the trial. We propose to measure eye-specific outcomes such as BCVA in both eyes throughout the trial, designating eyes as study eyes or not. Statistical analyses will take into account the availability of data for two eligible eyes in one patient. If both eyes present with CSCR at baseline, the clinical trial site will decide which is the primary eye and this eye will have retinal imaging performed first. The primary eye would usually be the one with most active disease/most subretinal fluid. It will be identified by OCT imaging and subsequent investigations such as fluorescein and indocyanine green angiography will then be performed initially on this eye. If a patient presents with one affected eye and the fellow eye subsequently develops CSCR the eye first affected will always be the primary study eye.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria

Exclusion criteria as of 12/01/2017:
1. Hyperkalaemia (serum potassium level > 5.0 mmol/L)
2. Hepatic or renal impairment (Patients with severe renal insufficiency (Estimated glomerular filtration rate, eGFR <30 mL per minute per 1.73 m2) or Patients with severe hepatic insufficiency (Child-Pugh Class C)
3. Pregnancy or breast feeding
4. Known allergy to fluorescein or indocyanine green
5. Patients receiving potassium-sparing diuretics, potassium-supplements, or inhibitors of CYP 3A4 (e.g.amiodarone, diltiazem, fluconazole, itraconazole, ketoconazole, ritonavir, nelfinavir, saquinavir clarithromycin, telithromycin, erythromycin, verapamil, spironolactone and nefazodone)). Patients taking furosemide are eligible.
6. Patients receiving the combination of an angiotensin converting enzyme (ACE) inhibitor and an angiotensin receptor blocker (ARB)
7. Patients receiving high doses of aspirin (>75mg)
8. Patients receiving nonsteroidal anti-inflammatory drugs (NSAIDs) (e.g. ibuprofen, naproxen).
9. Patients receiving lithium, cyclosporine or tacrolimus.
10. Hypersensitivity or known allergy to eplerenone or to any of the excipients.
11. Known hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption.

The following additional exclusions apply to a study eye only (i.e. they may be present for a non-study eye):
1. Evidence of choroidal neovascularization
2. Previous or current treatment with eplerenone for any reason or previous or current treatment with photodynamic laser therapy / any anti-VEGF therapy in the study eye / any intra-ocular steroid use / thermal laser therapy for CSCR
3. Presence of any other disease which could cause retinal fluid or SRF to accumulate (e.g. diabetic retinopathy, polypoidal choroidal vasculopathy, domed shaped maculopathy or choroidal haemangioma) or affect visual acuity
4. Myopia > -6 dioptres

Original exclusion criteria:
1. Hyperkalaemia (serum potassium level > 5.0 mmol/L)
2. Concomitant use of potassium-sparing diuretics or potassium supplements
3. Hepatic or renal impairment (Patients with severe renal insufficiency (Estimated glomerular filtration rate, eGFR <30 mL per minute per 1.73 m2) or Patients with severe hepatic insufficiency (Child-Pugh Class C)
4. Pregnancy or breast feeding
5. Known allergy to fluorescein or indocyanine green
6. Patients receiving potassium-sparing diuretics, potassium-supplements or strong inhibitors of CYP 3A4 (e.g. itraconazole, ketoconazole, ritonavir, nelfinavir, clarithromycin, telithromycin and nefazodone))
7. Patients receiving the combination of an angiotensin converting enzyme (ACE) inhibitor and an angiotensin receptor blocker (ARB) with eplerenone

The following additional exclusions apply to a study eye only (i.e. they may be present for a non-study eye):
8. Evidence of choroidal neovascularization
9. Previous treatment with photodynamic laser therapy / any anti-VEGF therapy in the study eye / any intra-ocular steroid use / previous thermal laser therapy for CSCR

10. Presence of any other disease which could cause retinal or SRF to accumulate e.g. diabetic retinopathy, polypoidal choroidal vasculopathy, domed shaped maculopathy or choroidal hemangioma
11. Myopia > -6 dioptres

Date of first enrolment
15/12/2016

Date of final enrolment
28/02/2018

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Study participating centre
Royal Victoria Hospital
274 Grosvenor Road
Belfast
United Kingdom
BT12 6BA

Study participating centre
Royal Blackburn Hospital
Haslingden Road
Blackburn
United Kingdom
BB2 3HH

Study participating centre
Bradford Royal Infirmary
Duckworth Lane
Bradford
United Kingdom
BD9 6RJ

Study participating centre

Royal Sussex County Hospital
Eastern Road
Brighton
United Kingdom
BN2 5BE

Study participating centre
Bristol Eye Hospital
Lower Maudlin Street
Bristol
United Kingdom
BS1 2LX

Study participating centre
Walsgrave General Hospital
Clifford Bridge Road
Coventry
United Kingdom
CV2 2DX

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

Study participating centre
Royal Liverpool University Hospital
Prescot Street
Liverpool
United Kingdom
L7 8XP

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

Study participating centre
Manchester Royal Eye Hospital
Oxford Road
Manchester
United Kingdom
M13 9WL

Study participating centre
Royal Victoria Hospital
Queen Victoria Road
Newcastle-Upon-Tyne
United Kingdom
NE1 4LP

Study participating centre
Royal Hallamshire Hospital
Glossop Road
Sheffield
United Kingdom
S10 2JF

Study participating centre
Southampton General Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre
Southend University Hospital
Prittlewell Chase
Westcliff On Sea
United Kingdom
SS0 0RY

Study participating centre
Sunderland Eye Infirmary
Queen Alexandra Road

Sunderland
United Kingdom
SR2 9HP

Study participating centre
Torbay Hospital
Lowes Bridge
Torquay
United Kingdom
TQ2 7AA

Study participating centre
New Cross Hospital
Wolverhampton Road
Heath Town
Wolverhampton West
United Kingdom
WV10 0QP

Study participating centre
York Hosptial
Wigginton Road
York
United Kingdom
YO31 8HE

Study participating centre
St. James' University Hosptial
Beckett Street
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LS9 7TF

Study participating centre
St Thomas’ Hospital
Eye Research Unit
Ophthalmology Department
Ground Floor
South Wing
St Thomas' Hospital
Westminster Bridge Road

London
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SE1 7EH

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

Study participating centre
Oxford Eye Hospital
LG1 West Wing
John Radcliffe Hospital
Headley Way
Oxford
United Kingdom
OX3 9DU

Sponsor information

Organisation
University Hospital Southampton NHS Foundation Trust

ROR
https://ror.org/0485axj58

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

Individual participant data (IPD) sharing plan
Anonymised individual patient data will be made available on request for secondary research, conditional on assurance from the secondary researcher that the proposed use of the data is compliant with the Medical Research Council Policy on Data Sharing regarding scientific quality, ethical requirements, and value for money. A minimum requirement with respect to scientific quality will be a publicly available pre-specified protocol describing the purpose, methods, and analysis of the secondary research (eg, a protocol for a Cochrane systematic review, approved by a UK research ethics committee or another similar, approved ethics review body). Patient identifiers will not be passed on to any third party. Requests should be made by email to the Chief Investigator: Professor AJ Lotery A.J.Lotery@soton.ac.uk.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	25/01/2020	24/01/2020	Yes	No
Results article		01/01/2021	14/06/2023	Yes	No
HRA research summary			28/06/2023	No	No
Other publications	retrospective cross-sectional study: genotyping for three central serous chorioretinopathy susceptibility single-nucleotide polymorphisms	01/05/2024	08/07/2025	Yes	No
Protocol file	version v6.0	20/03/2018	31/05/2018	No	No
Protocol file	version v7.0	25/02/2019	14/03/2019	No	No