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Patient Information Leaflet

The effectiveness of using Eplerenone to treat central serous chorio-retinopathy

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Trust study number (local site):
EME reference (if applicable): 13/94/15
IRAS No: 198007

Contact details

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Contents

PATIENT INFORMATION LEAFLET

VICI

The effectiveness of using Eplerenone to treat central serous chorio-retinopathy

We are a team of researchers who are conducting a study of a potential new treatment for an eye disease known as central serous chorio-retinopathy.

You are being invited to take part in this research study. Before you decide whether to take part or not, you need to understand why the research is being done, and what it would involve for you. Taking part in research is voluntary; it is up to you to decide to join the study. You are free to withdraw at any time, and if you choose not to take part or to withdraw from the research, you do not have to give any reason for your decision. Nobody will be upset, and the standard of care you receive will not be affected if you decide not to take part.

Please take time to read the following information carefully. **One of our team will go through the information leaflet with you, explain the study in more detail, and answer any questions you have**. If anything is not clear or you would like more information, do not hesitate to ask a member of the local research team (see contact details on page 2). Talk to others about the study if you wish, such as friends or relatives, and take time to decide. If you would like to take part, you will be asked to

confirm by signing a separate consent form and will be given a copy for your records.

What is the purpose of the study?
The purpose of this study is to look at the long term benefit of using a drug called eplerenone in the treatment of patients with an eye disease known as central serous chorio-retinopathy, or CSCR for short. Currently there are no proven treatments for this disease, but there have been some reports of patients having a good response to treatment with a drug called eplerenone. However, we do not know for sure if this treatment is effective because it hasn't been tested in a large group of patients, and it is currently unlicensed for treating CSCR. Some patients may get better anyway with no treatment, although this is less likely to happen in the chronic form of CSCR which is the form of the disease you have.

CSCR affects the retina which is the innermost part of the eyeball and which is the layer that senses light. In CSCR fluid collects between the retina and the other layers of the eye and this is an abnormal situation. Eplerenone works by removing this fluid.

Why have I been invited?
You have been invited to take part because your eye doctor has diagnosed CSCR. We aim to enrol 104 patients from all over the United Kingdom who have been diagnosed with CSCR.

What will happen to me if I take part?
If you agree to participate, after you have signed the consent form you will undergo tests to check that you are suitable for taking part in the study. If you are found to be suitable you will be randomised (that is randomly selected to one of the two arms of the study) to be treated with a capsule that is taken daily alongside your usual care. You will receive either the active treatment, which will be a capsule containing eplerenone, or a placebo treatment, which is a capsule that does nothing to you, but looks identical to the drug. We will compare the results in the eplerenone group against the results in the placebo group. The treatment will be given for up to twelve months. You and your doctor will not know which type of capsule you are receiving. This is to ensure that the results are not affected by the placebo effect (a positive effect on a condition caused by the patient's belief that a treatment will improve their condition) and that the research team are not subconsciously influenced by knowing if you are taking eplerenone or not. However, the research team can find out which type of capsule you have been receiving if required in an emergency.

A number of tests will be done during the trial, some at each check-up and some less often. You may already have had some of these tests as part of your usual care:

<u>Sight tests</u>
You will be asked to read letters from a chart under both normal and low light levels.

Ophthalmic Examination

Your pupils will be dilated with eye drops and special lenses will be used to look at your retina under high magnification. Please note that you must not drive until the effect of the eye drops on your vision has worn off. This can be several hours in some people. Therefore, it may be better for you to not drive to your appointments.

Autofluorescence, Fundus Photography and Fluorescein and Indocyanine Green Angiography

Bright flashes of light are used to obtain images of the retina. Some of these will be taken without any injection of dye. Then a special set of dyes called fluorescein and indocyanine green are injected into a suitable vein, usually in the arm or the back of the hand. When the dye enters the blood stream it flows through the blood vessels of the body including that of the eye, and the retina is photographed. The dyes allow us to clearly see the blood vessels and the amount of fluid behind the retina. The photographs are used to judge the type, extent and severity of the CSCR.

Optical Coherence Tomography

This procedure is used to examine the eye with beams of safe laser light. This test shows the thickness of the tissue layers inside the eye and how much fluid is present because of CSCR. This is important in monitoring the effects of treatment during the study.

Medical History

We will collect information about your medical history and other things like your age and if you smoke.

Physical examination

Your blood pressure and pulse will be measured at all visits.

Blood samples

Blood samples will be taken at each of your study visits. Tests done on these samples will help us to monitor for possible side effects, and understand the relationship between these side effects and the drug. We will take approximately 5-15 mls (a couple of teaspoons) for these tests which are essential to make sure it is safe for you to take part in the study and to continue taking the capsules during the study.

We are also asking your permission to take an additional blood sample, of about 30 mls (approximately 3 large spoonfuls), at your first visit, so that we can store the genetic material and other components from your blood for a future study. The genetic material is called DNA and contains information about your genes (characteristics you have inherited). We know that what genes people have can make them more susceptible to disease and can also affect how people respond to drug treatments.

The results of the tests on DNA will only be analysed for the entire group of patients. If any risks of relevance to you are identified during the process of carrying out these tests, this would be discussed with you if you have indicated that you would like us to. You do not have to agree to allow your genetic material to be studied. You can refuse to take part in this aspect of the research and still take part in the VICI study.

We also seek your permission to allow your DNA to be examined in future studies of eye disorders and related conditions. This is a developing area of research so we do not yet know in which studies your samples will analysed. However, one area of interest involves looking at how patients respond to treatment and genetic markers associated with different responses.

Blood samples for genetic analyses will be sent to the University of Southampton for processing and will be stored securely in a biobank. Research using the samples will only be conducted after approval by a Research Ethics Committee. You may request at any time that your samples are removed from the biobank and destroyed.

Safety

You will be given a card with a contact phone number which you should phone if you have any queries about your treatment or any possible side effects you may be experiencing.

Review visits

These will occur at 1 week, 4 weeks, 3, 6, 9, and 12 months, and if you agree to take part you will be required to attend all of these. At each of these visits, your eyes will be examined and some of the tests described above will be performed. You will also be asked about any side effects you may have experienced. The visits may take 3 hours each but also may be shorter.

It may be necessary for some patients to stop taking the capsules, either because their CSCR has improved or because of side effects. If this happens, we will ask you to continue to attend the reviews so that we can see how

your eyes are affected. Sometimes the tablets may be restarted and it that is the case we will repeat the visits at 1 week and 4 weeks.

What will I have to do?

Treatment

Whichever group you are allocated to you will be asked to take a capsule (which will either contain eplerenone or placebo but they will look identical) every day, preferably at the same time of day, for up to 12 months.
All participants will need to come back to clinic after a week for blood tests. This is because, if you have been given eplerenone, you will have been given a low dose to start with (25mg) to make sure you can tolerate it. If the blood test results are available whilst you are in clinic you will be advised then whether you can start the higher dose (50mg). If the blood test results are not back in time you will be given the higher dose capsules to take home but you MUST NOT start taking them until you have heard from the clinic that it is ok to do so. This process applies to all participants, as the study doctors do not know which patients are taking eplerenone and which are taking the placebo.

Questionnaires

During the trial you will be asked to complete a questionnaire, once at the beginning, and again at your 12 month visit. This is to let us know how your eyesight affects your life.

Expenses
We will refund you for any reasonable travel costs you have to pay to attend the clinic visits for the research.

What alternatives are there to taking part in the study?
If you decide not to take part in the research study, then you will receive whatever is the usual management of CSCR in your own hospital. This will vary between hospitals.

What are the possible disadvantages and risks of taking part?
The risks of taking part in the study include the risks of side effects from the eplerenone (see Appendix 1).

There are extra visits that you will need to undergo in excess of normal standard care and these visits may be slightly longer than usual. In addition, extra blood tests as described earlier will be needed in order to make sure your participation is safe.

If you consent to having blood taken for genetic material and other components to be examined in future studies you will have to undergo an additional blood collection at your first clinic visit.

Before consenting to take part you should consider if this will affect any insurance you have and seek advice if necessary. However it is very unlikely this would be the case.

What are the side effects of any treatment received when taking part?
Eplerenone may cause side effects but these are rare. In previous studies of CSCR, patients tolerated the drug well. For example, a pilot study that used eplerenone in 13 patients with CSCR for up to 3 months reported that none of the patients experienced any serious side effects from the treatment. Two patients reported fatigue and one patient a sedative effect. Blood tests remained in the normal range for all patients throughout the study. One possible side effect of eplerenone is a rise in blood potassium levels. However, we will carefully monitor for this side effect by testing your blood samples and take appropriate action if it occurs. In most cases, this would simply mean stopping the medication. A list of all possible side effects can be found in Appendix 1.

What are the possible benefits of taking part?
We cannot promise the study will help you but the information we get from this study may help improve the treatment of people with CSCR in the future.

What happens when the research study stops?
At the end of the study the data we collect will be analysed and we will let you know the results, if you wish to find out. We will also be able to tell you which group you were in. If the treatment is shown to have a positive effect and your doctor and ophthalmologist are happy to continue to monitor the effect in you, then you may be able to continue taking eplerenone (or start taking it if you were previously taking the placebo). However, as eplerenone is currently unlicensed for use in the

treatment of CSCR, even if it is shown to be beneficial, we cannot guarantee that it will be available to patients at the end of the study. Otherwise, when the study finishes you will be treated in accordance with standard practice at your hospital.

What if there is a problem?

If you have any concerns or questions about this study, please contact the research team listed on the inside front cover of this leaflet. Please feel free to ask any further questions before deciding to take part in the trial, or at any time during the study.

If you have concerns about the way you have been approached or treated during the course of the study, you may wish to contact the Patient Advice and Liaison Service (PALS) on:

<Insert local PALS details>

If you wish to make a formal complaint, please write to:

<Insert local details>

We have no reason to believe that you will be placed at any greater risk to your health by taking part in this research study compared to not taking part in this study. However, if something goes wrong and you are harmed during the research study there are no special compensation arrangements. The University Hospital Southampton NHS Foundation Trust cannot offer no-fault compensation and is unable to agree in advance to pay compensation for non-negligent harm. Ex-gratia payments may be considered in the case of a claim.

If anything goes wrong as a consequence of taking part in the trial because negligence has occurred, University Hospital Southampton NHS Trust, who is sponsoring the trial, will compensate you. Negligence would include, for example, a situation in which injury is caused by a deviation from the study protocol by the researcher. Your legal right to claim compensation for injury where you can prove negligence is not affected. If you are harmed and this is due to someone's negligence then you may have grounds for a legal action against the University Hospital Southampton NHS Trust, but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you.

In addition, if your vision deteriorates during the study, you doctor may discuss with you introducing other therapies such as laser treatments. At this time they may also discuss with you whether you should keep taking the study capsules.

Will my taking part in the study be kept confidential?
All information which is collected about you during the course of the research will be kept strictly confidential. We take the issue of confidentiality very seriously. In this study we will be collecting personal information such as your name, address and NHS number, to allow us to keep in touch with you during your participation in the research, and information about your health, to allow us to compare the two treatments. The data collected will be stored in a secure database held on the NHS network at the coordinating centre in Bristol, and will only be accessed by authorised members of staff involved in the

research. This includes the hospital research team and staff at the coordinating centre who are managing the research, all of which are bound by NHS rules of confidentiality. Paper copies will be stored in locked filing cabinets.

The images of the back of your eye will be transferred by a secure network to a specialist centre for analysis (Central Angiographic Resource Facility, Belfast). The images will be identified by a unique number known only to the study team so that no one looking at the images will be able to identify you by name or location

In addition, if you agree to have extra blood taken for genetic analyses, the samples that you give will be identified by a unique number known only to the study team so that no one doing the tests will be able to identify you by name or location.

Electronic data will be stored indefinitely on a secure database. These data will not have anything that could be used to identify you, and will only bear your unique study number.

If you give permission, the data collected maybe used for future ethically approved studies, but your personal details will not be released.

Your medical notes will need to be seen by authorised members of the hospital research team so they can collect information needed for this research study. With your consent, your GP will also be informed that you are

taking part in the research study. Your GP may be asked to provide information from your records which is required for the research. Occasionally, other members of NHS staff or research staff may need to check your medical records. This will be done by NHS staff or by researchers who are bound by the same rules of confidentiality as all NHS staff. The confidentiality of your medical records will be respected at all times. Under no circumstances will you be identified in any way in any report arising from the study.

What if relevant new information becomes available?
Sometimes we get new information about the treatment being studied. For example, other research may show additional side effects associated with eplerenone. If this happens, your research doctor will tell you and discuss whether you should continue in the study.
If you decide not to carry on, your research doctor will make arrangements for your care to continue.
OR
If you decide to continue in the study they may ask you to sign an agreement outlining the discussion.
OR
In light of the new information, your research doctor might consider you should withdraw from the study. He/she will explain the reasons and arrange for your care to continue.
OR
If the study is stopped for any other reason, we will tell you and arrange your continuing care.

What will happen if I don't want to carry on with the study?

You are free to withdraw from the study at any time you wish without giving a reason and without affecting your rights. You may just want to stop taking the study capsules and be happy to continue with the study visits so that we can monitor your progress, or you may want to withdraw from the study completely. This will be discussed with you at the time of withdrawal and you will also be asked whether you are happy for us to keep any of your samples that have been stored and any data collected so far.

What will happen to the results of the research study?

The results of the research will not be known until some time after the last patient has entered the study (about 3 years after the start of the study). The results may be reported in medical journals or presented at meetings but your identity will not be disclosed. During the course of the study we will ask you if you would like to receive a summary of the results by post after the research has finished.

Who is organising and funding the research?

The research is funded by the National Institute for Health Research. University Hospital Southampton NHS Foundation Trust has overall responsibility for conduct of the study. The research is being organised and run on their behalf by the Clinical Trials and Evaluation Unit, Bristol (CTEU Bristol).

Who has looked at the study?
All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your safety, rights, wellbeing and dignity. This study has been reviewed and given a favourable opinion by Wales Research Ethics Committee (REC) 1.

Further information
You can obtain **general advice on CSCR** and its treatment from The Macular Society,
PO Box 1870,
Andover SP10 9AD
https://www.macularsociety.org/
Helpline: 0300 3030 111
Switchboard: 01264 350 551

info@macularsociety.org

You can obtain **general information on clinical research** from the UK Clinical Research Collaboration (UKCRC) who produce a booklet called “Understanding Clinical Trials”. This provides in-depth information on the design and conduct of clinical trials and aims to answer the questions of those considering taking part.

A copy of this document can be requested from the research team or an electronic copy can be downloaded from the UKCRC website:
http://www.ukcrc.org/patients-and-public/public-awareness-of-clinical-research/information-resources-on-clinical-research/

Printed copies can be requested by emailing:
crncc.info@nihr.ac.uk

Or contacting:
UK Clinical Research Collaboration,
C/O Medical Research Council
One Kemble Street
London
WC2B 4TS
Tel: 020 7395 2271

Thank you for taking the time to read this leaflet

APPENDIX 1

Possible side effects of Eplerenone

In studies of patients with heart disease the following side effects were classified as ‘common’ (affect around 1 in 100 people):

- infection
- elevated potassium in the blood (symptoms include muscle cramps, diarrhoea, nausea, dizziness or headache; this will be monitored for during the study)
- dizziness
- fainting
- heart attack
- low blood pressure
- cough
- diarrhoea
- nausea
- constipation
- rash
- itching
- muscle spasms
- pain in the muscles, ligaments, tendons and bones
- kidney problems
- increased levels of a protein in the blood called urea, which could be due to kidney problems

The following are classified as ‘uncommon’ (affect around 1 in 1000 people):

- kidney infection
- sore throat

- raised levels of certain white blood cells
- underactive thyroid
- low levels of sodium in the blood
- dehydration
- increased levels of cholesterol or triglycerides (fats) in your blood
- insomnia (difficulty sleeping)
- headache
- numbness
- heart complaints (e.g. irregular heartbeat, fast heartbeat, and heart failure)
- thrombosis (blood clot) in the leg
- low blood pressure that can cause dizziness upon standing
- vomiting
- flatulence (wind)
- excessive sweating
- back pain
- cholecystitis (swelling or inflammation of the gall bladder)
- enlarged breasts in men
- general weakness and feeling unwell
- increased levels of a protein in the blood called creatinine, which could be due to kidney problems
- increased blood glucose
- other changes in other blood test results

In addition the following side effects have been reported in some patients but we do not know how common they are:

- Swelling of the deeper layers of the skin caused by a build up of fluid. This can affect any part of the body, but usually: eyes, lips, genitals, hands, or feet.

There may also be side effects that have not been identified yet.

A serious allergic reaction to this drug is unlikely, but seek immediate medical attention if it occurs. Symptoms of a serious allergic reaction include: rash, itching/swelling (especially of the face/tongue/throat), dizziness, trouble breathing.

If you suffer these or any other symptoms during the study please contact your local research nurse or doctor as soon as possible using the contact details on page 2, unless it is serious, in which case seek immediate medical attention.

For women
The effect of eplerenone during pregnancy and breast feeding is unknown in humans, therefore if you are pregnant or breast feeding, think you may be pregnant, or are planning to have a baby then you will not be eligible to take part in this study. If you are to take part in the study you must also be willing to use effective contraception, unless you are surgically sterile or have been post-menopausal for more than 12 months.

If, despite using contraception, you become pregnant during the study, you must inform the study team straight away using the contact details on page 2.