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EVRA (Early Venous Reflux Ablation) ulcer trial

A randomised clinical trial to compare early versus delayed endovenous treatment of superficial venous reflux in patients with chronic venous ulceration.

PATIENT INFORMATION SHEET AND INFORMED CONSENT DOCUMENT

You have been invited to take part in a research study called EVRA. Before you decide whether to accept, we would like to explain why the research is being done and what it will involve.

Please read this information carefully, and discuss it with others if you wish. Ask us if anything is unclear, or if you would like more information.

- *Part 1 tells you the purpose of this study and what will happen to you if you take part.*
- *Part 2 gives you more detailed information about the conduct of the study*

Take time to decide whether or not you wish to take part.

Thank you for reading this information sheet.

Part 1

What is the purpose of the study?

The EVRA study is for participants who have leg ulcers. A venous leg ulcer is a longstanding (chronic) wound on your leg or foot. These ulcers may either not heal or take a long time to heal and are usually caused by your leg veins not working very well. This problem with the veins is sometimes called varicose veins.

The usual care for venous ulcers is compression bandaging, followed by treatment of the varicose veins once the ulcer has healed. This study is being done to find out whether early treatment (within 2 weeks) of the varicose veins by modern keyhole (endovenous) procedures, in addition to compression bandaging, will help your leg ulcer heal quicker compared to the treatment with compression bandaging alone. Studies have shown that treating varicose veins can reduce the chance of an ulcer coming back, but we do not know if treating the veins early (within 2 weeks) will help your ulcer heal quicker.

Why have I been chosen?

Your doctor has invited you to consider this study because you have been diagnosed with a leg ulcer, which requires treatment to heal it. We hope about 500 people with leg ulcers will take part in this study from across the UK.

Do I have to take part?

No, participation in the EVRA study is entirely voluntary. If you do decide to take part you will be given this information sheet to keep. You will be asked to sign a consent form, but you are still free to withdraw at any time and without giving a reason. If you decide not to take part in the study, your doctor will be happy to talk through how he/she will treat your ulcer outside of the study. You don't have to give a reason for not taking part and your treatment and care will not be affected in any way.

What will happen to me if I take part?

The best way of finding out whether there are any advantages or disadvantages to this early treatment is by conducting a randomised study. 'Randomised' means that a computer will allocate participants randomly (as if by the toss of a coin) to receive either early compression bandages alone (with later treatment of the varicose veins), or early treatment of varicose veins by modern keyhole (endovenous) procedures in addition to compression bandages.

Neither your doctor nor you will choose which treatment you receive. In this way, a fair comparison can be made.

First Visit

If you decide to participate in the study, you will be asked to return for your first visit where you will be randomised and told which type of treatment you will have (i.e. compression bandages or compression bandages plus an early vein treatment). If you are randomised to early treatment of the veins, you will be booked for an appointment for the procedure within 2 weeks. If you are female and of childbearing age, a pregnancy test will be performed to confirm that you are not pregnant.

Whichever treatment you have, you will have a baseline assessment by the doctor or nurse to collect some information about your medical history and current condition, and take a tracing and photo of your ulcer to measure its size. The doctor or nurse will measure the ankle and arm blood pressures with a machine similar to an ultrasound to make sure the arteries are working normally in the leg.

Once you have given consent to take part in the EVRA study you will be asked to complete a confidential questionnaire pack about your quality of life. You will be asked to complete another pack again at your follow up visit at 6 weeks, and via post at 6 and 12 months after you entered the study. These questionnaires will help the research team to understand any problems you might experience after your treatment.

Follow-up visits

If you decide to take part in this study, the research team will collect information about your progress following your treatment up to 12 months, even if the ulcer heals before this. You will receive routine follow-up appointments in the community or at the hospital to monitor your progress and change your dressings. The research team will also collect information from these follow-up appointments about your ulcer and any complications that occur for 12 months from when you entered the study. A member of the research team will also contact you by telephone (around once a month) to ask you some questions and check how you are getting on. To ensure we collect reliable information from you regarding your bandage changes and visits with healthcare professionals we will ask you to complete a basic patient diary card to remind you of this information.

You will have one additional hospital visit at 6 weeks for assessment of your ulcer. Other than the 6-week leg ulcer clinic visit, the number of appointments is the same as treatment for your ulcer outside the study.

6 Week Visit

At the 6 week leg ulcer clinic visit you will have an assessment by the doctor or nurse to collect some information about your medical history and current condition, and take a tracing and photo of your ulcer to measure its size (just like the first visit).

If you are randomised to early varicose vein treatment you will also have an ultrasound scan at the 6-week hospital appointment to assess how well the treatment has worked. It is possible that the doctor may decide on further treatment depending on the results of the scan. For the purposes of this study, the ultrasound images and photos from your 6 week appointment will be taken and stored, and may be transferred to the Imperial College Trials Unit (ICTU) at the Imperial College London for review by a specialist. You will not be identifiable from your imaging.

As part of the follow up for the trial we ask that you contact the hospital or your nurse by telephone once you are told your ulcer has healed by the district / community nurse. The hospital will arrange for someone to visit you weekly (probably at home, but you may be asked to attend clinic) for 4 weeks to take a photo just like your first and 6 week visit. This photo will be anonymised and sent electronically to the Imperial College Trials Unit so that experts can confirm that your ulcer is fully healed.

There are no restrictions on your activity when you are in this study. You will continue with any other medical care or treatments, such as taking regular medication, as you would normally do. There are no limitations on you seeking other medical advice, if you need to, whilst you are taking part in this study.

What is the intervention that is being tested?

If you agree to take part in EVRA you will be treated with standard therapy for venous leg ulcers (compression bandages, with later treatment of varicose veins), or the standard compression bandages plus an early varicose vein treatment (within 2 weeks).

Varicose vein treatments:

There are several different ‘early treatments’ for your varicose veins. Your doctor will discuss the different options with you in detail, and help decide the best way to treat them. The two main ways of treating your veins in the study are briefly described below.

1) Radiofrequency or laser ablation

Varicose veins may sometimes be treated by heating the wall of your varicose vein using either radiofrequency or laser energy. The vein is accessed through a small cut, usually made just below the knee. The procedure is usually carried out with the patient awake using local anaesthetic, where a painkilling injection will be used to numb the area being treated. A small radiofrequency or laser fibre is then passed into the vein and positioned at the top of your varicose vein to be treated. Some more local anaesthetic is then injected around the vein and the fibre heats the vein, causing it to close off and seal shut. Once the vein has been sealed shut, your blood will naturally be redirected to one of your healthy veins. The entire procedure is performed with the help of ultrasound scanning.

2) Foam Sclerotherapy

Varicose veins may sometimes be treated by injecting a special type of foam into the affected vein (foam sclerotherapy). The foam scars the veins, which seals them closed. The injection is guided into the vein using an ultrasound scan and is usually carried out under local anaesthetic. Following sclerotherapy, your varicose veins should begin to fade. Foam sclerotherapy may also be performed in addition to radiofrequency or laser ablation procedures.

What are the alternatives forms of treatment?

Your varicose veins could be treated with a traditional stripping operation, which involves tying off the vein in the affected leg and then removing it. This is usually carried out under general anaesthetic, which means you will be asleep during the procedure. You would usually be able to go home the same day, however, in some cases an overnight stay in hospital may be necessary. Following the procedure, you may need between one and three weeks to recover before returning to work.

Each of the keyhole vein procedures have advantages and potential disadvantages, but are less invasive than traditional open surgery and have replaced surgery in many hospitals. Traditional surgery will therefore not be offered as part of this trial.

What is the standard treatment?

Standard treatment consists of multilayer compression bandages or stockings to get the ulcer to heal, followed by treatment of varicose veins to reduce the chances of the ulcer coming back.

Multilayer Compression Bandages / Stockings

There are many different types of bandage used to treat venous leg ulcers. Studies have shown that multilayer bandages work better than single layer and therefore all patients in the EVRA study will be treated with these (or stockings with a similar compression). Multilayer compression bandages will lead to about 65% of ulcers healing within six months. The application of a compression bandage is a skilled procedure and should be done by a healthcare professional trained in leg ulcer management. Bandaging of the leg is usually done after a leg ulcer dressing change. The bandage and ulcer dressing can then remain in place for up to one week, depending on how often ulcer dressing changes are required.

Treatment of varicose veins

Treatment of varicose veins (using one of the procedures described previously) has been shown to reduce the chance of the ulcer coming back. In many hospitals, traditional operations to remove varicose veins have been replaced by modern 'keyhole' endovenous procedures such as laser ablation, radiofrequency ablation or foam sclerotherapy. These procedures are usually offered to patients once their ulcer is healed.

Unwanted effects of treatment

Whilst these treatments used in the EVRA study are done very frequently, all medical procedures carry risks of complications. Possible complications of both compression bandages and endovenous procedures are listed below. These are only the complications which could occur; we are not expecting them all to happen to you.

Radiofrequency or laser ablation may cause:

- some short-term side effects such as numbness or pins and needles (paraesthesia).
- some tightness in your legs and the affected areas may be bruised and painful.
- nerve injury is also possible, but usually only temporary.

- blood clots in other leg veins (DVT)

Sclerotherapy can have side effects, including:

- blood clots in other leg veins (DVT)
- headaches
- changes to skin colour, for example, brown patches over where the treated veins were
- fainting
- temporary vision problems, and very rarely strokes.

After any of these procedures, it is possible that you may develop a painful lump over the varicose veins, known as phlebitis. This may require treatment with antibiotics and/or drainage.

Compression bandages:

Side effects of compression bandages are uncommon. Whilst we do not anticipate any specific side effects as a result of taking part in this trial, in extremely rare circumstances, some patients may be allergic to materials that are contained within the bandages. If this is the case, we will use another product which does not contain that material. Other complications are:

- some discomfort
- in rare cases, skin ulcers may be caused by compression treatment in patients with fragile skin or artery disease

Pregnancy: It is important to let your doctors and nurses who are looking after you know if you are pregnant or become pregnant as it may affect your care. During the course of the study if you find out or suspect you may be pregnant you must tell your doctor as soon as possible.

How is my condition monitored?

Participating in the EVRA study will not significantly affect how your ulcer is monitored or any other treatment you receive for it. Your ulcer will be monitored by regular visits to your GP community hospital or district nurse and they will notify you when they think your ulcer has healed.

The follow up visits required for the study are decided by your doctor and are similar to what would normally be done (usually monthly), with the exception of the 6 week clinic visit. Information about your disease and any complications that occur will be collected at your first visit, and then monthly for 12 months by the nurse reviewing your notes and a monthly telephone call. You will be asked to complete a patient diary card every time you visit a health professional so we can collect information on your bandage changes and number of visits with health professionals. You will be asked to fill in questionnaires about your quality of life on your first visit (baseline), and at 6 weeks and at 6 months and 12 months after randomisation. Information required at other time points will be obtained from your medical records. With your permission, we will collect information on your progress for several years.

What are the possible disadvantages and risks of taking part?

All of these treatments are routinely offered to most patients with venous leg ulcers, and therefore the risks of taking part in this study are the same as the risks of having treatment outside of the study.

What are the possible benefits of taking part?

The information gained from the study may help doctors and patients make future decisions as to the best approach (early endovenous treatment compared to standard therapy of compression bandages) to treating venous ulcers in the future.

What if I do not want to take part?

If you do not wish to take part in the study your doctor will discuss with you how he/she will treat your ulcer. This will usually involve standard compression bandages and treatment of your varicose veins by either surgery, radiofrequency / laser ablation or foam sclerotherapy, usually once your ulcer has healed.

What happens when the research study stops?

The information from the EVRA study will be used to decide if compression bandages alone or compression bandages plus an early procedure to treat varicose veins is the best way to treat leg ulcers. In addition, the research team will also use the information collected to compare the safety and cost of the two types of treatment and the amount of care needed by participants after the treatment.

What if something goes wrong?

A group of independent researchers (the Data Monitoring Committee) will closely monitor the study. If there are any problems then they will be detected as soon as possible so that the study can be changed or stopped if necessary.

Will my taking part be kept confidential?

If you decide to participate in EVRA, the information collected about you will be handled strictly in accordance with the consent that you have given and also the 1998 Data Protection Act. Please refer to part 2 for further details.

This completes Part 1 of the Information Sheet. If the Information in Part 1 has interested you and you are considering participation, please continue to read the additional information in Part 2 before making any decision.

Part 2

What if relevant new information becomes available?

Sometimes we get new information about the treatments being studied. If this happens your doctor will discuss with you how this affects you.

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

You can decide to leave the study at any time. You do not need to give a reason.

If you leave the study before your treatment then your doctor will discuss with you what type of treatment he will use outside the EVRA study

If you decide to leave the study after the treatment then your data collected up until that time will remain on file and will be included in the final study analysis and follow up information will continue to be collected from your medical records.

If you decide to leave the study and do not wish for any further data to be collected about you, you should inform your clinical care team of this in order that no further follow up information is collected from your medical records.

In line with Good Clinical Practice guidelines, at the end of the study, your data will be securely archived. For the purpose of the EVRA study, data will be archived for a minimum of 10 years after which arrangements for confidential destruction will be made.

What if there is a problem?

Complaints:

If you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal local complaints services are available to you.

For UK participants, complaints will be dealt with via the National Health Service. These are unique to your local NHS trust and your study doctor or nurse can give you their information.

Harm:

Imperial College London holds insurance policies which apply to this study. If you experience serious and enduring harm or injury as a result of taking part in this study, you may be eligible to claim compensation without having to prove that Imperial College is at fault. This does not affect your legal rights to seek compensation.

If you are harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study then you should immediately inform the Investigator (Insert name and contact details). The normal National Health Service complaints mechanisms are also available to you. If you are still not satisfied with the response, you may contact the Imperial AHSC Joint Research Compliance Office.

Will my taking part in this study be kept confidential?

If you decide to participate in the EVRA study the information collected about you during the course of the study will be handled in accordance with the consent that you have given and the 1998 Data Protection Act. You data will be stored for a minimum of 10 years following completion of this trial.

All information which is collected about you during the course of the research will be kept strictly confidential. Any information about you which leaves the hospital will have your name and address removed so that you cannot be recognised from it

Your data will be entered onto a secure database held at the ICTU in accordance with the 1998 Data Protection Act.

With your permission, your relevant medical records may be inspected by authorised individuals from the research team or Imperial College London (the study Sponsor). They may also be looked at by the relevant regulatory authorities to check that the study is being carried out correctly.

Involvement of the General Practitioner/Family Doctor (GP):

With your permission, your GP, other doctors involved in your clinical care and your community nursing team will be kept informed of your participation in the EVRA study, but otherwise all information about you and your treatment will remain confidential.

What will happen if I lose mental capacity during the study period?

This is expected to be a very rare occurrence. If this did occur we would like to continue to collect safety and follow up data about you from your medical records via your clinical care team and would like you to let us know on the consent form if you would be happy for this to occur.

What will happen to the results of the research study?

When the study is complete the results will be sent to all trial participants and published in a medical journal, but no individual participants will be identified.

Who has organised, reviewed and funded the research and who will be supervising it?

This research grant has been awarded by the Health Technology Assessment Programme, which is funded by the National Institute for Health Research. 'The sponsors of this study will pay [*enter name of hospital department*] to cover the costs of your participation in this study.

The research is being co-ordinated centrally by the Imperial College Trials Unit (ICTU) at Imperial College (UK). The ICTU has overall responsibility for coordination of the study. The research has been reviewed by all of these organisations and an independent National Research Ethics Committee; The NRES Committee South West - Central Bristol REC.

Contact Details

If you have any further questions about your disease or clinical studies, please discuss them with your doctor. You may also find it helpful to contact the research nurse on *(insert telephone number*).

If you would like further information about clinical research, the UK Clinical Research Collaboration (a partnership of organisations working together on clinical research in the UK) have published a booklet entitled 'Understanding Clinical Trials'. Contact UKCRC: Tel:0207 670 5452; website:www.ukcrc.org/publications/informationbooklets/

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Participant Trial ID:	Initials:
Date of Birth:	NHS Number:

EVRA Study

PATIENT CONSENT FORM

Please initial each box

1. I confirm that I have read and understand the information sheet dated 06/01/2014, (Version 2.0) for the above study and have had the opportunity to ask questions. ☐

2. I understand that my participation is voluntary and that I am free to leave the study at any time without my medical care or legal rights being affected. ☐

3. I understand that relevant sections of my medical records may be looked at by authorised individuals from the research team, from regulatory bodies, from the study Sponsor, or from the NHS Trust in order to check that the study is being carried out correctly. I give permission, provided that strict confidentiality is maintained, for these bodies to have access to my medical records for the above study and any further research that may be conducted in relation to it. ☐

4. I understand that even if I decide to leave the above trial, the data collected about me will be used in analysing the results of the study. I understand that my identity will remain anonymous. ☐

5. I agree to allow any information or results relating to the safety and monitoring of this study to be used for healthcare and/or medical research purposes. I understand that my identity will remain anonymous wherever possible. ☐

6. I agree to the imaging from my ultrasound being sent to the Imperial College Trials Unit and then to an independent assessor for review. I understand that I will not be identifiable from the images. ☐

7. I understand that my personal data will be stored securely in an Imperial College facility for a minimum of 10 years. ☐

8. I agree to my GP, or any other doctor treating me, being notified of my participation in this study. ☐

9. If during the study my clinical care team determine that I have lost capacity to provide informed consent, I give an advance decision that I would wish to remain in the study. I understand that no further study procedures will be carried out on me in this event, but I am willing for the collection of safety and follow up information from my medical records to continue. ☐

10. I agree to long-term follow-up in the event that the trial is extended and that further information about my health status may be obtained from the Health and Social Care Information Centre. ☐

11. I agree to take part in the EVRA study. ☐

Full Name of participant	Date	Signature

Name of Person taking consent	Date	Signature

(1 copy for participant; 1 copy for the patient's medical notes, 1 copy for the site file)