University Hospital Southampton NHS
NHS Foundation Trust

Using cardiovascular magnetic resonance identified scar as the Benchmark Risk Indication Tool for Implantable cardioverter defibrillators in patients with Non-Ischemic Cardiomyopathy and Severe systolic Heart failure (BRITISH)

Contents

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We invite you to take part in a research trial

You have been given this information sheet because we would like you to think about taking part in the BRITISH Trial.

You are being invited to take part in the BRITISH trial because you have been diagnosed with heart failure.

Before you decide whether or not to take part, it is important for you to understand as much as possible about what is involved, so:

- Please take your time to read this information carefully. You may also wish to discuss it with your family and friends before making up your mind.

- Please feel free to ask your doctor any questions you may still have after reading this information sheet.

Do I have to take part? No. It is entirely up to you if you take part in the trial or not. If you choose not to take part, the care you get from your own doctors will not be affected in any way.

If I start the trial, can I stop if I want to? Yes. If you choose to take part in the trial, you are free to stop at any point without giving a reason – the standard of your care will not be affected.

Introduction

Thank you for considering taking part in the BRITISH Trial.

This research trial is being done so we can better understand how to treat patients like you who have been diagnosed with a certain type of heart failure. If you decide to take part in this trial:

- You will need to sign a consent form to confirm you understand it and agree to take part.
- We would like your permission to collect, store and analyse link-anonymised data about you so we can learn about the best ways to manage patients who have the same type of heart failure as you.

Link-anonymisation is achieved by linking your personal identifiable information to your unique study identification number. Only your hospital and the Southampton Clinical Trials Unt will hold this information.

Before you decide whether to take part, we would like you to understand why the research is being done and what it would involve for you. One of our team will go through the information sheet with you and answer any questions you have.

1. Why are we doing the BRITISH Trial?

Heart failure and its risks

Heart failure means that your heart is not pumping blood around your body as effectively as it should.

Having heart failure doesn't mean that your heart has stopped working, but that your heart needs some support to help it work better.

Heart failure can be caused by a blood supply problem where the heart arteries are diseased or blocked. This is known as Ischaemic Cardiomyopathy. Heart failure can also be caused by other conditions *not* related to the blood supply and this is known as Non-Ischaemic Cardiomyopathy.

The BRITISH trial is investigating whether we can improve the way we treat patients like you who have non-ischaemic cardiomyopathy (NICM).

Some patients with NICM have a higher risk of experiencing serious abnormal heart rhythms that might be life threatening. Current guidelines recommend doctors consider fitting a device that can correct these serious abnormal heart rhythms. This device is called an Implantable Cardioverter Defibrillator (ICD). However, we know from previous research studies that a lot of patients – perhaps as many as 90% - who have an ICD never need to use it because they won't experience any serious heart rhythm abnormalities.

We want to try and work out which patients will benefit from having an ICD and which patients are better off not having an ICD. We want to try to make the guidelines more specific. This could be better for patients and hospitals.

What is an ICD?

An Implantable Cardioverter-Defibrillator is a device which is implanted under the skin under a local anaesthetic. It has a battery/generator component and leads which are fixed into the heart chambers. It has the ability to detect dangerous heart rhythms if they occur and deliver a shock to treat this to help prevent sudden cardiac death.

Having an ICD fitted does however carry with it a risk of problems developing e.g. bleeding, infection, lead problems and inappropriate shocks. Research data has shown that these problems can be as common as *1 person in every 6* with an ICD.

What do we know so far?

Evidence gathered across several studies from about 20 years ago showed that fitting an ICD reduced the risk of death in patients with heart failure. It was on this evidence that the current guidelines were developed. These studies included heart failure patients who had ischaemic (caused by diseased heart arteries) heart failure and non-ischaemic (not caused by diseased heart arteries) heart failure.

A recent large trial (called 'DANISH') of over 1000 patients with severe Non-Ischaemic Cardiomyopathy, has called the current guidelines into question. In the DANISH trial, patients were randomised to either have an ICD fitted or to have no ICD fitted.

The trial concluded that for patients who received an ICD, there was no difference in the likelihood of dying when compared to patients that didn't have an ICD fitted. This means that patients who were fitted with an ICD were overall, *not* better off in the long term.

Looking at the data from the DANISH trial, there are clues that *some* patients may still benefit from an ICD, even though the headline results suggest they are not necessary. It's likely that it's the patients who are at increased risk of having a serious abnormal heart rhythm that stand to benefit from ICDs.

What are our current practices?

Following the publication of the DANISH trial, surveys across Europe and the UK have found that nearly 50% of Cardiologists have changed their practice as a result of DANISH. Although the current guidelines still recommend fitting an ICD in patients with severe heart failure, the majority of doctors now implant ICDs in less than three quarters of patients with this type of heart failure.

This means that after the DANISH trial, *there is no agreement on what the best treatment is and individual clinicians are making their own decisions for their patients with Non-Ischaemic Cardiomyopathy*. As a result, many doctors are deciding ***not*** to implant an ICD in patients with this type of heart failure, as they believe there is no overall survival benefit.

What are we trying to determine?

Research has shown that patients who have scar tissue in their heart, seen on Cardiac Magnetic Resonance Imaging (CMR), are at a higher risk of dying suddenly from an abnormal heart rhythm. We would like to test whether the presence of scar tissue on the heart scan (CMR) can be used to decide if patients need an ICD or not.

All participants in this study have Non-Ischaemic Cardiomyopathy with evidence of scar tissue on CMR. The trial will randomly assign (like the toss of a coin), half the trial participants to receive an ICD and the other half to no ICD.
For those participants that are allocated to no ICD, we'd like to fit a device called an Implantable Loop Recorder (ILR), as a safety mechanism for study participants. This procedure is explained in more detail later in the information sheet.

Both groups will be followed up to decide whether having an ICD fitted reduces the chances of people dying from an abnormal heart rhythm.

Currently, there is no agreement on how best to decide which patients with Non-Ischaemic Cardiomyopathy actually need an ICD. The BRITISH trial aims to answer this question. The information gained from this research has the potential to change treatment guidelines and improve how patients with this condition are managed around the world.

2. What would be involved if I decide to take part?

If you decide to take part in the trial, you will be asked to sign a consent form which confirms that you agree to take part. The original consent form will be filed securely at the hospital, and you will be provided with a copy. A copy will be kept in your medical notes, a copy sent to the Southampton Clinical Trials Unit (SCTU) via secure e-mail and held securely. At the end of the trial the original consent form will be archived by the hospital who took consent for a period of 15 years. The copy sent to the SCTU will be destroyed as confidential waste prior to the trial being archived.

Following consent, you will have initial assessments (called screening) to make sure that you that you meet all of the eligibility criteria. This is to ensure that this trial is suitable for you.

If you are eligible to take part in the trial and you agree to take part you will randomised (assigned by chance) to 1 of 2 arms of the trial:

i) Group 1: ICD fitted
or
ii) Group 2: No ICD fitted

If you're in group 2 – No ICD fitted - we will use an Implantable Loop Recorder (ILR) to record your heart rhythm instead.

What is an Implantable Loop Recorder (ILR)?

An ILR is a tiny implantable device which sits under the skin and monitors your heart rhythm. The ILR cannot deliver a shock or treat any abnormal heart rhythms. The Cardiac Rhythm Management team are able to access information from the ILR remotely and act on any significant findings if required.

If certain abnormal heart rhythms are detected, your clinical team will decide whether you need to have an ICD fitted. If this happens, you will continue in the trial and have the trial follow-up. Your safety is of paramount importance.

Regardless of which group you are in, you will continue to be managed and followed up as normal by your clinical team.

Cardiac Resynchronisation

Sometimes with heart failure, the heart's pumping action can become disorganised and it doesn't pump blood around the body efficiently. To correct this, some heart failure patients require a special three-lead pacemaker as part of their treatment. This is known as a Cardiac Resynchronisation Therapy (CRT) pacemaker.

If you need to have a CRT pacemaker, then your clinical team will have discussed this with you. You will still be eligible to take part in this trial but it's important you have a device that corrects your hearts pumping action. This can be done with either a pacemaker that can also shock the heart to correct a serious abnormal rhythm (CRT-D) or with a pacemaker that only paces your heart and records the rhythm (CRT-P).

If you need cardiac resynchronisation and decide to take part in BRITISH, you will receive a CRT-D instead if you are randomised to group 1 and a CRT-P instead if you are randomised to group 2.

The research would involve having the following investigations:

● Cardiac Magnetic Resonance Imaging (CMR) scan

You will have a CMR scan of your heart as part of your normal care. This will be used to determine if there is scar tissue present on your heart. However, for this study we would like to ask your permission to share these scans with the Barts Heart Centre at St Bartholomew's Hospital, London, for centralised analysis. Your MRI scan will be link-anonymised by your treating hospital. The scan will be coded with your unique study identification number and any information that may identify you will be removed, before the scan is sent to the Heart Centre. The Heart Centre will undertake specific measurements and calculations on heart scans for all patients in the study. This will provide important information and help to decide which patients might benefit most from having an ICD fitted in the future.

● Blood Tests

If you consent to take part in BRITISH, we would ask to take some blood from you.

One blood test will be done to measure your blood sugar level, and another will provide information on how severe your heart failure is. These blood samples will be taken after you have consented to take part in BRITISH. Both can be taken with routine clinical blood tests but if taken on their own, the amount of blood we will need is less than 10mls (approximately 2 teaspoons). The tests will provide important clinical information on all patients in BRITISH and will be described in the final study results. The blood samples will be destroyed as per your hospital's policy after analysis and will not be stored long-term for research purposes.

We will also ask for an extra blood sample to be taken for research purposes. The extra sample will be link-anonymised and stored for research at a central storage unit. This sample will be collected at the same time as your routine clinical blood tests. The amount of blood required will be approximately 10mls. The blood samples may be used for genetic analysis, but any results will not be used to inform your management or recorded in any of your medical notes.

● Kansas City Cardiomyopathy (KCCQ-12) questionnaire

The KCCQ-12 is a short questionnaire asking some questions about any heart failure symptoms you may have and how they affect daily activities. You will need to complete this once you have consented to take part and in 3 years time, during the follow-up telephone consultation with the research team.

● **EQ-5D-5L questionnaire**

A short questionnaire consisting of 5 questions to evaluate your quality of life in the following areas:

- mobility
- self-care
- usual activities
- pain/discomfort
- anxiety/depression.

You will need to complete this once you have consented to take part and in 3 years time, again during the follow-up telephone consultation.

We will remove your personal details from the information we collect about you for the trial. We will, however, keep some identifiable information about you. This will allow us to make regular checks on trial participants. At certain time points during the trial we will check your health status. This will be done remotely. We won't need to contact you to find this out. The study team will continue to collect data, regarding your health status, until the end of the trial. The end of the trial will be when the final patient recruited to the BRITISH trial reaches their 3 year follow up visit.

If you have any concerns about any of the investigations, there is a team of specialists available for you to talk to. This team includes Doctors, Physiologists and Nurses.

3. Will I be followed up during the trial?

You will be followed up by your clinical team as part of your routine care. This is not part of the trial but will be decided by your own personal needs. We would like to telephone you for the trial once, 3 years after you have joined to see how you

are and to check what tablets you're taking. At this point we will go through the same questionnaires as detailed above.

Sometimes research studies don't run to completion. If BRITISH stops early for any reason, you will be informed by your research doctor. Your ongoing care will be tailored by your clinical care team to meet your personal needs.

Device Follow-Up

Any device you have fitted will be checked wherever possible, remotely via a home monitor by the Cardiac Rhythm Management team as per standard care. You will receive training and information on this before you go home after the device implantation.
Sometimes, it is required for you to attend in person for device checks, but this will be guided by the team at your hospital. This information will be recorded as part of the trial follow-up. The research team will liaise directly with your clinical team, so you won't need to do anything extra for this to happen.

Long term Follow-Up

We would like to ask for your consent to access your data via NHS Digital (or equivalent) for up to 10 years after the last patient has been followed up in the trial. This will be done remotely, and we will not need to contact you. NHS Digital collects data from across health and social care in England and there are equivalents for Wales and Scotland. For patients in Scotland, your Community Index Number (CHI) number will be used. With your consent, during the trial, NHS Digital, or the applicable service in your area, will provide certain information about your health status to the SCTU upon request. The SCTU is registered under the Data Protection Regulations to hold such information on a confidential basis.

4. What will happen to the research data once the trial has finished?

The research data collected during this trial will be securely stored for up to 15 years following completion of the trial for this purpose.

As our understanding of heart failure evolves, we may use the link-anonymised research data collected during this trial to support prospective heart failure research projects. This may include securely sharing the link-anonymised research data with other national and international research teams and institutions who are conducting similar studies in heart failure.

No personal information will be transferred – that's to say, all your private details will be removed before information is shared. This includes things like your name and address.

5. What are the possible risks and disadvantages of taking part in the trial?

Risks associated with an ICD

Whether you decide to take part in the research trial or not there are risks associated in having an ICD fitted. The trial will not increase or decrease any risk around this procedure. Your clinical team will discuss the potential risks involved with you as part of the consent process.

Common complications include bleeding (2.6%), infection (at time of implant or at a later date – this can require removal of the device) (1.7%), pneumothorax (air leaking around the lungs) (1.7%), tamponade (blood leaking around the heart) (0.8%), failure to implant a lead in the correct place or movement of a lead after, requiring revision (3.1%). There is a 2-3% risk of inappropriate shocks which can occur after the implant (when the device interprets your heart rhythm as dangerous and issues a shock you don't need). All these risks combined total around 1 in 6.

You will undergo a procedure using X-rays to fit the ICD and afterwards to check the position of the ICD. These procedures use ionising radiation to form images of the inside of your body. Ionising radiation can cause cell damage that may, after many years or decades, turn cancerous. As you would have a similar procedure if you did not take part, the chances of this happening to you are the same whether you take part in this trial or not

If you are randomised to No ICD, it's likely you will have an Implantable Loop Recorder (ILR) fitted (unless you require a CRT pacemaker).

Risks associated with Implantation of an ILR

The risks of an ILR are very small. There is a small (<1:100) risk of bruising/bleeding and infection (which may require removal of the device). Rarely, the device cannot sense the heart rhythm properly and needs to be moved. In total the risk of ILR implant is <2% of any complication.

If you need cardiac resynchronisation therapy, you will either have a CRT-D (group 1) or a CRT-P (group 2) fitted.

Risks associated with implantation of CRT-D

This is the same as that described for ICD implant above.

Risks associated with implantation of CRT-P

This is the same as that described for ICD implant above, except there is no risk of inappropriate shocks.

6. What are the possible benefits?

There may be no personal benefit for you if you decide to take part in this trial. We hope there may be some benefit to patients in not having an ICD fitted if they don't need one. However, we can't be sure of this and this is why we're doing the trial.

Even if there is no personal benefit to you in taking part, we hope this trial will increase our knowledge and improve how we manage patients like you in the future. We hope the trial results might lead to a change in the guidelines used by doctors when they decide which heart failure patients should have an ICD fitted.

7. What are the alternatives to taking part in the trial?

If you prefer not to take part in the BRITISH Trial, your doctor will be able to discuss the alternative options with you. Please be reassured that it is entirely up to you

whether or not you decide to take part in the trial. If you decide not to take part, the standard of your care will not be affected in any way.

8. Other questions you may have about the trial:

What does informed consent mean?

No one can enter you in a clinical trial without your permission. To help you decide if taking part in a clinical trial is right for you, the trial doctor/nurse will discuss the trial with you in depth. The most important thing is that you should feel satisfied that you know enough about the trial to make an informed decision. You should feel free to ask as many questions as you need to. In addition, you should be given as much time as you need to make your decision - you should not feel rushed.

How will we use information about you?

We will need to use information from you, from your medical records and your GP for this research project.
This information will include:

- Your name
- Your NHS number (CHI number for patients in Scotland)
- Your contact details

We will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

We will keep all information about you safe and secure.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

The SCTU will keep non-identifiable information about you for 15 years after the study has finished.

[Insert name of local NHS site] will keep identifiable information about you from this study for 15 years after the study has finished.

What are your choices about how your information is used?

- You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.
- If you choose to stop taking part in the study, we would like to continue collecting information about your health from central NHS records, your hospital and your GP. If you do not want this to happen, tell us and we will stop.
- We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.
- Your MRI heart scan will be stored at the Barts Heart Centre and the research blood sample you provide stored at a central storage unit. Scans and samples will be link-anonymised by your local hospital prior to leaving the hospital.

Where can you find out more about how your information is used?
You can find out more about how we use your information from the following sources:

- Sponsor's data protection officer: Email: dataprotection@uhs.nhs.uk Telephone: 023 8120 4743
- By accessing the Health Research Authority website at: www.hra.nhs.uk/information-about-patients/
- By accessing the Health Research Authority leaflet available from the following link: **www.hra.nhs.uk/patientdataandresearch**

Will my details be kept confidential?

Yes. University Hospital Southampton NHS Foundation Trust (UHSFT) is the sponsor for this trial based in the United Kingdom. Individuals from UHSFT, SCTU and regulatory organisations may look at your medical and research records to check the accuracy of the research trial. Your hospital will pass these details to the SCTU, along with the information collected from you and your medical records.

The only people in UHSFT and the SCTU who will have access to information that identifies you will be people who need to use this information for follow-up purposes, to enable the research team to access your data via NHS Digital (or equivalent), or those who audit the data collection process. This will allow the trial to report on long term follow-up.

Will my General Practitioner be informed?

With your permission, we will tell your General Practitioner (GP) that you are taking part in the BRITISH Trial. Your medical records will be available to those involved in your clinical care and authorised individuals from the Sponsor or the Sponsor's delegates from the SCTU, Funder and Regulatory Authorities.

Risk for women of childbearing potential

Pregnant women are excluded from this trial. If you think you may be pregnant you must inform your doctor. If you become pregnant during the trial:

- Prior to device implantation – you will no longer be eligible for device implantation
- After device implantation – you may continue on the trial.

What if there is a problem?

If you decide to take part in the BRITISH trial and feel concerned about any part of the trial at any point, you should contact your research doctor/nurse as soon as possible. Your research team will do their best to help you and answer your questions.

If you wish to complain or have concerns about any aspect of the way that you have been approached or treated during the BRITISH trial, the normal NHS complaints system will be available to you. If you are harmed due to someone's negligence, then you may have grounds for legal action but you may have to pay legal costs.

You have the same rights as any other NHS patient.

If you have private medical insurance you may wish to check with your provider before agreeing to take part in this trial to make sure that your participation will not affect your cover.

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

If you decide to take part in BRITISH then you are still free to withdraw at any time without giving a reason. This will not affect your future care in any way but we would still like to know how you are, and with your permission, will request this information from your doctor. This is so that the overall quality of the study is not impaired. Please let your doctor know if you wish to withdraw and he/she will carry on your care in the normal way.
If you withdraw, you will be asked to clarify which part of the trial you are withdrawing from. You may withdraw from some parts or all parts. Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. Any blood samples that you have previously provided will be retained.

Who is organising the research and has it been reviewed?

The research is sponsored by UHSFT and co-ordinated by the Southampton Clinical Trials Unit. All research in the NHS is also looked at by a Research Ethics Committee, to protect your interests. This trial has been approved by Fulham Research Ethics Committee, London.

How will I be informed about the results of this trial?

After the trial is completed, all results will be examined and a report submitted for publication in a medical journal. You will not be identified in any report or publication. It may take a number of years for the results of the trial to be known. When the trial has completed, the results will be sent to your study doctor, who will be asked to pass on the results of the study to you.

How have patients and the public been involved in this trial?

A Patient and Public Involvement (PPI) group has been actively involved in giving feedback on the BRITISH trial design and reviewing the patient literature. Our research team has greatly appreciated their opinions and have made necessary amendments according to their suggestions.

9. Contact Information

If you have any further questions about your condition or available treatments please discuss them with your doctor. If at any stage you have questions about the BRITISH trial, or would like to discuss your participation in more detail, please contact:

Investigator names: ***(insert local PI details – name and address - and contact numbers)***

Telephone number:

Thank you for reading this Participant Information Sheet – please ask any questions if you need to.

(To be printed on local headed paper)

INFORMED CONSENT FORM – BRITISH RCT

Using cardiovascular magnetic resonance identified scar as the **B**enchmark **R**isk **I**ndication **T**ool for **I**mplantable cardioverter defibrillators in patients with Non-Ischemic Cardiomyopathy and **S**evere systolic **H**eart failure (BRITISH)

Patient Identification Number for this trial: | | | | — | | | | | | | | |

Name of Researcher:

		Please initial box
1.	I confirm that I have read and understand the information sheet dated 07-Feb-2023 (version 6.0) for the above study and I fully understand what is involved in taking part in this trial. I have had the opportunity to consider the information, ask questions and these have been answered satisfactorily.	INITIAL
2.	I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason and without my medical care or legal rights being affected.	INITIAL
3.	I give permission for a copy of my consent form to be sent to the Southampton CTU (where it will be stored securely), to allow confirmation of my consent.	INITIAL
4.	I understand that sections of my medical records may be looked at by responsible individuals from the research team at the University of Southampton, by the sponsor (University Hospital Southampton NHS Foundation Trust) or by regulatory authorities, for the purposes of this research and its management. I give permission for these people to look at my medical records.	INITIAL
5.	I understand that the information collected about me may be used to support other research and may be shared with other researchers once link-anonymised.	INITIAL
6.	I agree to my General Practitioner being informed of my participation in the study and that the study team can contact my GP should they need to clarify clinical data needed for study purposes.	INITIAL
7.	I consent to give research blood sample(s) for analysis including genetic analysis.	INITIAL

8. I understand that link-anonymised Cardiac Magnetic Resonance Imaging scans will be sent to the Barts Heart Centre.	INITIAL
9. I understand my details will be registered with the National Health Service Digital or equivalent for which my name and NHS number or equivalent must be used in order for my health status to be followed up.	INITIAL

10. I agree to take part in the BRITISH study.	INITIAL

Name of Participant	Signature	Date
Name of researcher taking consent	Signature	Date

When completed:

- 1 for participant;
- 1 for researcher site file;
- 1 (original) to be kept in medical notes;
- 1 copy should be sent to the SCTU via a secure nhs.net account to uhs.sctu@nhs.net, or using the University of Southampton's SafeSend service (if participant provided consent for this)