Participant Information Sheet

Distal ventricular pacing and intraventricular gradient reduction for symptomatic relief in drug-refractory hypertrophic cardiomyopathy patients with mid-cavity obstruction

We invite you to take part in this research study

You have been invited to take part in this research as you have an inherited cardiomyopathy which can be very difficult to treat. We believe your symptoms are mostly caused by obstructed blood flow which leads to high pressures within the heart. There are currently very few treatment options beyond taking medicine, which may not help in reducing symptoms. We have developed a new technique which uses a cardiac pacemaker to try to reduce obstruction and abnormally high pressures within the heart and think this may relieve your symptoms.

Before you decide, 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. We would suggest that this should take about 30 minutes. Talk to others about the study if you wish. If you agree to take part in this study, we will then ask you to sign a consent form.

What is the purpose of the research?

We want to test whether the pacemaker can reduce the abnormally high pressures within the heart. When it is fitted, we will measure the effect pacing has on the obstruction and pressures. We know, from a group of patients who have already had this experimental procedure, that it improves some patients' symptoms a lot, other patients' not so much, and some patients' not at all. Because of this, we need to see if there is a benefit to the patient from having the pacemaker set up in a certain way.

What would taking part involve?

Taking part in this study will involve recording the information at: a pre-implant visit; a visit for cardiac device implantation; and follow-up visits six and twelve months later. The number of visits is the same as the standard care you would receive if you were not taking part in the study. However, the number of non-invasive tests you need will increase as part of this research study. The main differences between having the device offered as usual care (clinically) and as part of the study (research) have been summarised in the table below:

	Device offered **clinically**	Device offered as **research**
Device implant procedure with pressures measured within the heart, and overnight stay	Yes	Yes
Randomisation into groups for 6 months	**No**	**Yes**
6 month follow-up appointment	Yes	Yes
Exercise test, blood sample, and symptom assessment via questionnaire at 6 month follow up	**No**	**Yes**
12 month follow up appointment	Yes	Yes
Exercise test, blood sample, and symptom assessment via questionnaire at 12 month follow up	**No**	**Yes**
Patient aware of pacemaker settings for first 12 months	**Yes**	**No**
Increased risk of research participation	No	No

Pre-implant visit: after giving informed consent, you will undergo assessment of your symptoms and physical performance. This will be done with health-related questionnaires and exercise testing with walking and a bike. We will also take a small blood sample to test for a protein that we think is linked to your heart condition. The whole process should take around the same time as a normal visit to the Cardiomyopathy Clinic, between two to three hours.

Device implantation: we will record pressures within your heart using a catheter (long tube), whilst placing pacing leads on the right and left side of the heart. The special type of pacemaker is called a biventricular device and has three leads. Biventricular device implants typically take up to two and a half hours. The time of the procedure is unchanged by taking part in the research. If during the procedure no abnormal pressures are demonstrated, you will not be suitable for the study. We will plan to implant a more conventional pacemaker or defibrillator if this is needed for other reasons. The more conventional device will almost always be one that does not include the additional left ventricular lead.

Overnight stay: After having a device implanted, it is standard care that the patient stays overnight in hospital, before travelling home the next day.

12 month follow-up period: The second element of the research study is what happens the day after the pacemaker implant. If you agree to take part in the study, you will be randomly allocated to one of two groups. One group will have the pacemaker set up to pace all the time (active pacing), and one group will be set up for back-up pacing only (very little pacing). We will not tell you which group you are in as this might affect the way you describe your symptoms. We will again assess your symptoms and physical performance at a visit to the hospital six months later. You will then have the pacemaker switched to the other setting for six months (either active pacing or back-up pacing depending on which you had first).

At the end of the second six month period, we will again assess your symptoms and performance. That will conclude your part of the research study, at which point we will tell you about your pacemaker settings and leave you in the setting in which you feel better.

What are the clinical alternatives?

The treatments for patients with your heart condition that have severe symptoms are very limited, but include medicines and cardiac transplant. The use of a pacemaker

in this situation is an experimental treatment which has not yet been explored in a randomised clinical trial. The pacing therapy is available to you without taking part in the research study. We want to test if this treatment works using a “clinical trial”.

Who decides which treatment group I go into first?

We do not know which treatment method is generally better, which is why we are conducting the study. As a participant, you will experience both a treatment period (active pacing) and a non-treatment period (back-up pacing). Once you have experienced both settings, we can compare how you felt. The order in which you experience each setting is not decided by your doctor or the research team, but by randomly assigning you to one or other first.

Setting your pacemaker to active or back-up pacing will not affect the defibrillator function of your device if it has one. If your doctor or the investigator thinks you may be at higher risk of sudden cardiac death, you will have a device fitted with defibrillator functions as well as the pacemaker functions. If your doctor or the investigator thinks that you are not at risk of sudden cardiac death, the device you have fitted may have pacemaker functions only.

We will make every effort to shield you from knowledge of your pacemaker set-up for the follow-up period of 12 months. At the end of the 12 month period, we will ask you in which of the two six month periods you felt better in. You will then be told of your pacemaker settings.

Why am I eligible to take part?

You have been referred for pacemaker implantation, with or without a defibrillator, by your consultant in the Cardiomyopathy Clinic. You are someone who we believe may have symptomatic benefit from using the pacemaker function of the device, but we would like to test that in this study.

What happens to my blood samples?

Your blood samples will be made anonymous and destroyed after testing for the protein is complete.

Will I be exposed to higher risks if I take part?

When implanting this type of device, there is a 1-3% risk of infection, 1% risk of blood clot on the lung, and around a 5% risk of lead displacement in the long term. However, this device is being implanted as part of your standard care, and the

research element of the procedure does not increase the risk. Interference with a nerve which can cause a muscular twitching sensation in the abdomen occurs in around 10% of patients having a left ventricular lead implanted, and this is known as phrenic nerve stimulation (PNS). When PNS occurs, it can usually be avoided by careful programming of the device.

What are the possible benefits of taking part?

We cannot guarantee that your symptoms will improve as part of this study. However, patients with your condition have very few treatment options available to them if medication doesn't ease your symptoms. Initial tests of using a pacemaker for your condition have been very encouraging, so this research may change how we treat patients all over the world with your heart condition.

What are the possible disadvantages and risks of taking part?

• ***Side effects of treatments / therapies*** We do not expect any significant side effects as part of the research study. If you feel unwell you can get in contact with the research team.

• ***The discovery of new health-related findings***

If we find any unexpected health-related findings as part of this research, they will be shared appropriately with you and the clinical team responsible for your care.

Further information

• ***What if something goes wrong?***

If you experience anything that causes you concern, or you have questions about the research, a research related-injury, or compensation, during this study you may contact the study doctor or the research team on the numbers below with any issues.

• ***What will happen if I do not want to carry on with the study?***

You can withdraw from the study at any time without giving a reason. If you decide to stop being in the study, we will keep the information we have already collected about you, and use it for the study, unless you tell us you want all your study information withdrawn. If you are finding it difficult to manage your symptoms during the follow-up period, you can contact the Cardiomyopathy clinic team, as well as directly with the study investigator (numbers at the bottom of this information sheet). The

research team has regular direct contact with the clinical team responsible for your care, and any concerns raised can be discussed immediately. Further, a trial safety committee will meet quarterly to review safety aspects of the trial and those patients whom are in various stages of the follow-up.

If you wish to withdraw before the follow-up period is complete, we would ask you during which time you felt less symptomatic, before unmasking you to your pacemaker settings. You would then be left in the setting in which you felt better, be it active or back-up pacing.

If your symptoms worsen to the extent that your clinician is considering offering cardiac transplant, taking part in this study will not affect the timing of that referral.

• How will my information be kept confidential?

We will keep your information confidential both on paper in the trial master file, under lock and key in the Cardiovascular Research Unit, and electronically, in a password-protected database.

• What will happen to the results of this study?

The results of the study will contain no patient names and no information that could be associated with any individual patient. You will be informed of the results via letter unless you opt out of further correspondence. The results will be spread within the wider research and clinical community via presentations and publication in journals.

• Who is organising and funding this study?

The research is organised and managed by the research team at the William Harvey Research Institute and Barts Hospital. The study is funded by a research grant from the National Institute of Health Research.

• Will I get paid for taking part?

Participants will not be paid for taking part in this study.

• How have patients and the public been involved in this study?

Patients and the public were actively involved from the very early stages of this study, for example: in its design; in the review of the application to the funding body; and in writing study documents such as this patient information sheet. We have set up a trial steering committee that includes two patients from similar clinical backgrounds as you, to continue receiving input and advice from patients as the study progresses.

• Who has reviewed this study?

To protect your interests, all research in the NHS is looked at by an independent group of people called a Research Ethics Committee. This study has been reviewed and given a favourable opinion by a Research Ethics Committee (London – Harrow, REC Reference 17/LO/1725). The study has also been approved by the Research & Development department at your hospital.

• What should I expect during the consent process?

Written consent will be taken by a member of the research team, after you have been given due time to discuss and understand the information provided in this Participant Information sheet about the study, and consider if you want to take part.

• Will my General Practitioner be involved?

With your permission on the consent form, your GP, and other doctors who may be treating you, will be notified that you are taking part in this study.***• How do I get further information?***

If you want any further information about the study, you can contact a member of the research team on **020 3765 8635**.

The trial manager, Dr Vivienne Monk, is available to answer questions during office hours on **020 7882 5668**.

If you have specific concerns or wish to raise a complaint about the conduct of the trial, the hospital complaints department can be contacted on Patient Advice and Liaison services (PALS) telephone number: **020 3594 2040**.

If you decide you would like to take part then please read and sign the consent form. You will be given a copy of this information sheet and the consent form to keep. A copy of the consent form will be filed in your patient notes, and the original will be filed with the study records.

Thank you for taking the time to read this information sheet and to consider this study.