IMMUNE-DCM Study

Participant Information Sheet

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Principal Investigator: *<to be inserted>*

Chief Investigator: Professor Ioakim Spyridopolous

An observational study to understand the links between IMMUNE cell biology and Dilated CardioMyopathy patient characteristics.

Invitation to taking part in this clinical study

You have recently or previously been diagnosed with a type of heart condition called dilated cardiomyopathy (DCM) and we would like to invite you to take part in a research study that is including patients with DCM.

Before you decide whether you want to take part, it is important that you understand why the research is being done and what taking part involves. This information sheet explains why we are carrying out the study, and what will happen to you if you choose to be involved in this study.

One of our research team will go through this information sheet with you and answer any questions you have. It is important that you take time to read and understand the following information. Please ask us if there is anything that is not clear. If you decide that you would like to take part, we will ask you to sign a consent form.

You are under no obligation to take part in this study, and if you do, you are free to stop at any time. Your on-going care will not be affected if you decide not to participate or if you decide to stop.

What is the purpose of the study?

Dilated cardiomyopathy, or DCM, is a disease of the heart muscle which makes the muscle walls become stretched and thin (dilated). The thinner walls are weakened, and this means the heart can't squeeze (contract) properly to pump blood to the rest of the body. Each side of your heart has an upper chamber (your atria) and a lower chamber (your ventricles). DCM affects the lower left chamber (ventricle) of your heart. The job of your left ventricle is to pump the blood with a new supply of oxygen to the rest of the body.

Research has shown that DCM is caused by either genetics or environmental triggers, like infections, drug or alcohol use, or by high blood pressure leading to inflammation. This inflammation is generated by the body's own immune system.

Studies have suggested that certain immune system cells (called T-cells or T-lymphocytes) with a particular immune receptor called CX3CR1 may be involved in causing damage to the heart. Immune receptors sit on the outside of cells and act like channels to allow things to pass in and out of cells. There is a study currently taking place to assess how safe and how well a drug blocking the CX3CR1 receptor works in patients that have had a heart attack, to stop further heart damage. Our own research has shown that there are more immune receptors in patients with dilated cardiomyopathy. This suggests that the process that causes heart damage leading to a heart attack, could be the same as the way that the heart becomes weakened in DCM.

This clinical study aims to recruit 100 or more patients who have DCM to study this process. This study will help to strengthen our understanding of the DCM disease process and help us to design a drug study in the future. Patients will be recruited from the Newcastle Upon Tyne Hospitals & South Tees Hospitals NHS Foundation Trusts.

This study is also being undertaken as part of a degree, being undertaken by the research fellow.

What will happen to me if I agree to take part in this study?

If you are eligible and agree to take part, at your first (baseline) visit:

- You will have your blood pressure, heart rate, height, weight, and Body Mass Index (BMI, which we will calculate from your height and weight) measured.
- We will perform a heart rhythm scan called an electrocardiogram (often called an ECG).
- We will take a medical history and perform a physical examination of you to check your current health.
- You will have a patch (see **Figure 1)** that can monitor your physical activity (like a step counter), heart rate and rhythm fitted on your upper chest. We will then ask you to perform a sit to stand test that will last 1 minute*

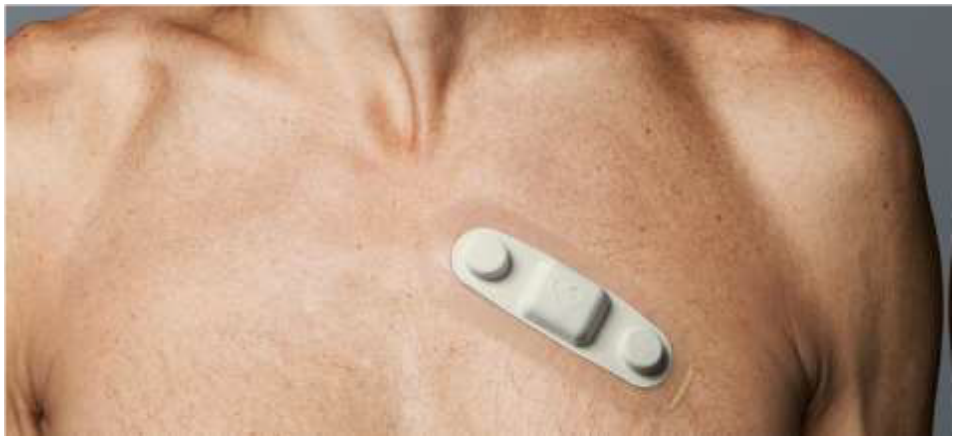

Figure 1 Vivalink patch attached to upper part of chest

- We will also take a swab from your throat to test for viruses, these will include HIV, Hepatitis B, Hepatitis C, Covid, Influenza Adenovirus, Parvovirus B 19, Respiratory Synctial Virus, Enterovirus, and Coxsackie virus,
- We will ask you to complete a questionnaire, called the Kansas City Cardiomyopathy Questionnaire.
- We will make arrangements for you to return to the hospital to have blood tests and a cardiac Magnetic Resonance Imaging scan (cardiac MRI), which normally takes about 2-6 weeks to arrange, but occasionally this may occur

earlier and may even be able to occur at this baseline visit. The MRI scan produces detailed still and moving images of the heart, its valves and blood vessels without using radiation. These images will be used to look at the shape and function of the heart and its structures. Cardiac MRI is regularly used to detect or monitor different cardiac conditions, and you may have had one already. We will use a dye known as a contrast agent so that the images of blood flow to your heart show up more clearly on the scan, this will be injected into your arm through a vein.

- If you have an MRI scan on this visit, we will also take blood tests. We will insert a needle, called a cannula to take blood from you for us to carry out a number of tests. The blood sample will take approximately 80 ml of blood, which is about 13 teaspoons. We will use this to measure your blood counts (including red blood cells and haemoglobin), markers of inflammation, virus antigen/antibodies** and to look at different immune cells in your blood. This will also include a genetic assessment, where we will look at your DNA to see if there are markers that are associated with DCM. Your blood tests and appointment will ideally be scheduled in the morning. If so, we would recommend you fast overnight until your blood tests are done.

*: The patch may be attached at baseline or at visit 2. A courier service will be arranged by us to pick up the watch/patch or this can be posted back to the hospital department. We will provide details at the time.

**: The blood tests will include tests to assess the presence of HIV and Hepatitis virus antigen and antibodies. The results of these tests will remain confidential and the results will be shared with you.

<u>Visit 2 within 0-6 weeks of your first (baseline) visit (this visit may not be required if the MRI and blood test happen at baseline).</u>

- If not already performed at the baseline visit. We will insert a needle, called a cannula to take blood from you for us to carry out a number of tests. The blood sample will take approximately 80 ml of blood, which is about 13 teaspoons. We will use this to measure your blood counts

(including red blood cells and haemoglobin), markers of inflammation, virus antigen/antibodies** and to look at different immune cells in your blood. This will also include a genetic assessment, where we will look at your DNA to see if there are markers that are associated with DCM. Your blood tests and appointment will ideally be scheduled in the morning. If so, we would recommend you fast (no food, or drinks other than water) overnight for 8-12 hours until your blood tests are done.

- You will undergo a cardiac MRI scan that same day. More information about the MRI scan is a little later in this information sheet.
- You will have a patch that can monitor your activity (like a step counter), heart rate and rhythm fitted on your upper chest. We will then ask you to perform a sit to stand test that will last 1 minute*

Visit 3 - approximately 6 months after your MRI visit

- You will have your blood pressure, heart rate, height, weight, and BMI measured.
- We will perform an ECG.
- We will take a medical history and perform a physical examination on you.
- You will have a patch that can monitor your activity (like a step counter), heart rate and rhythm fitted on your upper chest. We will then ask you to perform a sit to stand test that will last 1 minute*
- We will ask you to complete the same questionnaire (called the Kansas City Cardiomyopathy Questionnaire) you answered at baseline again.
- We will take a blood sample (approximately 80 ml, about 13 teaspoons) to measure your blood counts, degree of inflammation, and look at different immune cells in your blood. Your blood tests and appointment will ideally be scheduled in the morning. If so, we would recommend to you an overnight fast until your blood tests are done.

Where possible, your study visits will be timed to coincide with your normal hospital follow-up appointments. Members of the study team will make these appointments with you.

You may be contacted at 12 months by a member of the study team via telephone as part of a 12 month follow up visit. The purpose of this contact will be to contact you to clarify if you have had any heart related health issues since the last study visit. Consent for this visit will be sought in the informed consent form. This is subject to further funding.

*: The patch will be attached in the same way as it was earlier in the study to your upper chest. A courier service will be arranged by us to pick up the watch/patch or this can be posted back to the hospital department. We will provide details at the time.

**: The blood tests will include tests to assess the presence of HIV and Hepatitis virus antigen and antibodies. The results of these tests will remain confidential and the results will be shared with you.

Do I have to take part?

No, it is entirely up to you to decide whether you want to participate in the study.

Will it affect my future medical care if I decide not to take part and what happens if I change my mind?

No, deciding not to take part will not affect your future medical care.

If you decide to take part, you may withdraw at any time. You do not have to give a reason, but it is helpful to the study if you do give us some feedback in case we can make any changes to improve the study for others.

If you decide to withdraw completely, data collected up to the point of withdrawal will be retained and used for analysis. You will be asked about whether further information may be collected from your medical notes and if any samples collected for further research might still be used.

Withdrawing from the study will not affect the care that you receive.

Should I take my medicines as usual?

Yes. Please take your usual medicines as normal. As part of your medical history check, your cardiologist will have discussed your current medications with you. If you needed to stop any medications or take new or more medications, your cardiologist looking after you will have already discussed this with you as part of your routine care.

Do I need to tell my GP?

No, if you become a study participant, with your permission we will send your GP a letter informing them that you are taking part in the study. This is so that your medical records at your GP practice and in the hospital contain documentation that you are taking part in a clinical study. If you need to see your GP for anything during the study, please remind them that you are taking part in a research study. We may also contact your GP if we need any information about you during the study that is not available from your medical notes at the hospital.

What happens if I feel unwell?

If you feel unwell at any time, please contact your GP or cardiologist. It will also be important that the cardiology research team know about any problems that you have, so please make sure you that you also keep them informed by contacting them on the number at the end of this information sheet. If you experience a medical emergency, you should seek medical attention as you would normally.

Are there any risks to my health?

There is no study medicine, but there are some minor risks involved with taking part in this research which are outlined below.

What are the risks associated with taking blood?

Risks associated with taking a sample of blood from your arm include pain, bruising, light-headedness and on rare occasions, infection.

What are the risks associated with the wearable devices?

The wearable devices will be a heart monitor patch attached to your upper chest. You will have this device attached to your upper chest for about a week, and can wear it for all activities including bathing. It will allow us to record your heart rate, rhythm, and physical activity levels during the week. It should not cause you any harm or discomfort.

What are the risks associated with having a heart scan (MRI)?

A cardiac MRI scan is a non-invasive test that uses an MRI machine to create magnetic and radio waves to show detailed pictures of the inside of your heart. You will be asked to lie on a bed which moves inside a tunnel-shaped scanner. The scanner is open at both ends. You will be asked to lie still while the scan is taking place. The scan may last for up to 30 minutes, but there is a buzzer you can press if you need to speak to the person operating the scanner. The

scanner is quite noisy. You will be able to hear banging sounds but you will usually be offered earplugs or earphones so you can listen to music.

The contrast dye will be injected into a vein in your arm. You might experience an allergic reaction to the dye and need treatment. This occurs very rarely.

Your doctor will give you more information about this if it is required. If you are claustrophobic (afraid of being in small spaces), tell your doctor before the test. You may be offered a mild sedative - a medicine to help you relax. There are no risks for an MRI scan and few side effects, if any. The test does not use ionising radiation, and to date, there have been no documented side effects from the radio and magnetic waves it uses. Allergic reactions to the dye are rare.

The MRI scan would not be part of your usual care.

Will I receive and travel expenses and payments?

Reasonable travel expenses will be available for the study visits. Reimbursement will be provided only for study visits that are outside your routine clinical care. Your study team will manage any payments to reimburse costs to you and you may be asked to provide receipts for your travel.

No additional payments will be made for taking part in the study.

What are the possible benefits of taking part?

There may be no immediate personal benefit from taking part in the study but the information we get may help improve the understanding of the disease process affecting patients with DCM. This may form the basis of a new drug trial to explore new treatments in DCM. You will receive additional follow-up following your diagnosis compared to that of routine care, including blood tests, heart rhythm monitors and a cardiac MRI scan.

How will we use the information about you?

We will need to use information from you and your medical records.

This information stored will include:

- Name
- Date of birth
- NHS number
- Contact details

This information will be held at the hospital site. People 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.

This means your data will be link anonymised. Only the study team at your hospital will be able to link this number back to you using your date of birth, name and NHS number.

Some parts of your medical records and the data collected for the study may be looked at by authorised persons from the study management group (which includes members of the Academic Cardiovascular Unit at South Tees Hospitals NHS Foundation Trust who are helping to co-ordinate the study) and Sponsor (Newcastle upon Tyne Hospitals NHS Foundation Trust) to check that the study is being conducted to the correct standards. All will have a duty of confidentiality to you as a study participant.

Your data which leaves the NHS Trust where you are being treated will be stored both electronically and in paper form; during the study this will be held securely in databases, operated by third parties, but accessible to the research team.

Once we have finished the study, we will keep some of the data (for at least 5 years) so we can check the results. We may use this data for future research. We will write our reports in a way that no-one can work out that you took part in the study.

Following the end of the study, we will send the de-identified data to the funder of this study AstraZeneca. This would include sending your Unique Subject ID, sex, ethnicity and age.

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 and your hospital. 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.

If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study.

What will happen to the blood samples collected?

Some blood samples will be sent to the local hospital laboratory for analysis, once a result has been confirmed, any remaining sample will be destroyed in line with routine hospital practice. Other blood samples collected will be sent to the Clinical Genetics & Genomics Laboratory at Imperial College London and the National Horizons Centre at Teesside University for genetics assessment,

and the Centre for Life in Newcastle-upon-Tyne for research analysis (see **Figure 1** below). Some of the blood samples remaining after analysis may be used for further testing to help identify a potential future heart failure drug, these samples may be sent to AstraZeneca, who are funding this study.

Blood samples will be kept for a maximum period of 5 years after the end of the study, after which they will be destroyed. They will be kept in a licenced Newcastle University Biobank. **Your consent to store these additional samples in a biobank is optional**. Your biobank samples may be used in further research linked to this study. Your samples can only be identified by using your code number. Researchers who use your samples will not know who you are.

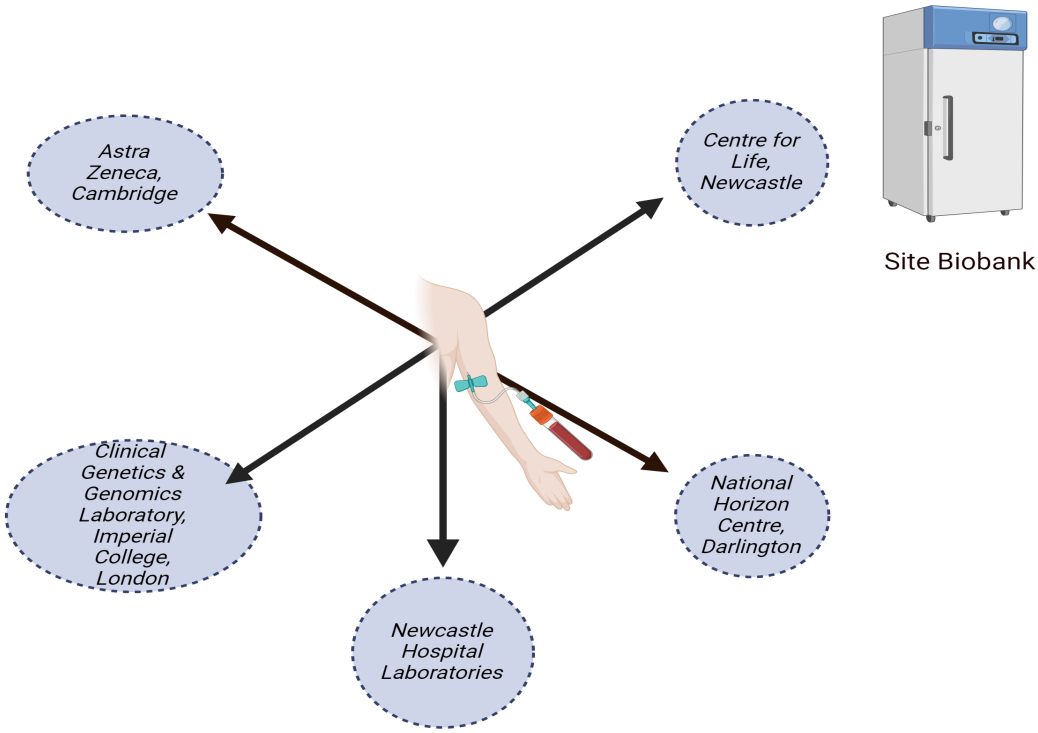

Figure 2 Figure to illustrate where your blood samples will go, if you take part in the study. Long term storage of some blood tests will occur at the Centre for Life biobank.

What will happen to the results of the study?

Having collected all the results, we will study the immune and inflammatory response within your blood and heart during the 6 months. Should any of the genetic blood tests or tests for viruses show results that may affect your or you or your family's future health, you may be referred to a (genetic) counsellor to help you think through what the results mean for you and your family.

The results of the study will be written in medical journals and presented at meetings to other doctors, nurses, researchers and patients. A report will be written for the study funder. All study data that is published will be anonymous. Your identity will always be protected.

The results will be available at the end of the study through publications, in the wider press and directly to patient groups. If you choose to consent, you will be sent a copy of the summary of the results from your study hospital.

Who has reviewed the study?

The study has been reviewed by Wales REC 7,NHS Research Ethics Committee. The Committee needs to be satisfied that your rights will be respected, that any risks have been reduced to a minimum and balanced against possible benefits, and that you have been given sufficient information on which to make an informed decision to take part or not.

Who is organising and funding the research?

The study is the responsibility of the sponsor which is the Newcastle-upon-Tyne Hospitals Foundation Trust. The research team also includes a wider team of cardiologists and researchers from the Academic Cardiovascular Unit at the James Cook University Hospital in Middlesbrough and researchers and

cardiologists from Newcastle University and the Freeman Hospital in Newcastle, England. This study is funded by the company AstraZeneca which is based in Cambridge, UK.

What if something goes wrong?

If you are harmed by taking part in this research, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for legal action, but you may have to pay for it. Regardless of this, 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 National Health Service complaints mechanisms are available to you.

If you prefer to raise your concerns with someone not involved in your care, you can contact the Patient Advice and Liaison Service (PALS). This service is confidential and can be contacted on Freephone: 0800 032 0202

Alternatively, if you wish to make a formal complaint you can contact the Patient Relations Department through any of the details below:

Telephone:

Email:

Address:

WHERE CAN YOU FIND OUT MORE ABOUT HOW YOUR INFORMATION IS USED?

You can find out more about how we use your information

- at www.hra.nhs.uk/information-about-patients/
- in our leaflet available from https://www.newcastle-hospitals.nhs.uk/help/privacy/privacy-notice-for-patients/by asking one of the research team

- by sending an email to the Sponsor Data Protection Officer at nuth.dpo@nhs.net

- by ringing the Newcastle upon Tyne Hospital Data Protection Officer on 0191 223 1474

Contact for further information

For further information regarding the study, to tell us that you would like to withdraw from the study or if you wish to discuss any matters related to the study with a member of the research team, please contact us as detailed below:

Enter full address of recruiting NHS Trust

Enter contact details of lead Cardiologist at the recruiting NHS Trust

Enter contact details of the main research team contact for the study at the recruiting NHS Trust

You can also contact the Research and Development Department at the Trust for general advice using the following details:

Enter contact details of the R&D department at the recruiting NHS Trust

Thank you for taking the time to read this information.