ISRCTN17189947 https://doi.org/10.1186/ISRCTN17189947

A study to link IMMUNE biology with the features of patients with the heart condition dilated cardiomyopathy

Submission date 26/04/2024	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol
Registration date 02/05/2024	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 04/06/2024	**Condition category** Circulatory System	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims
Dilated cardiomyopathy, or DCM, is a disease of the heart muscle which makes the muscle walls become stretched and thin (dilated). When the thinner walls are weakened, it means the heart can't squeeze (contract) properly to pump blood to the rest of the body. DCM affects the lower left chamber of your heart (called the left ventricle). The left ventricle usually has thick, muscular walls. With DCM, the enlarged, thinner muscle walls give the heart a rounder shape rather than its usual cone shape.
Research has shown that DCM has either a genetic and/or an environmental cause including infections which can trigger an inflammatory process. This process is called an immune-mediated inflammatory response, and research shows it is partly caused by the interaction between the amino acid Fractalkine and its receptor CX3CR1. Common infections which have been associated with starting this immune process are the cytomegalovirus (CMV), HIV and Hepatitis virus to name a few. We aim to perform an observational and feasibility study, to better understand the relationship between this immune-mediated inflammatory response with common DCM genetic mutations, CMV, HIV and hepatitis viral status, the patients' signs, symptoms, degree of heart failure as well as the extent of inflammation and scarring on the heart. This observational study may then give us an understanding of whether specific groups of patients with dilated cardiomyopathy might benefit from a drug targeting the CX3CR1 receptor, which will help us to design future trials.

Who can participate?
Adults over 18 years, with dilated cardiomyopathy.

What does the study involve?
We aim to recruit 100 patients with dilated cardiomyopathy and split them into 2 groups based on their degree of pump failure. We aim to do so as research has shown that the clinical course and disease process in patients with DCM differs, when split based on clinical features including, the degree of heart pump failure. This process of splitting the groups is called phenotype clustering. We will take consent and then perform tests at each initial (baseline) visit and at 6 months, as well as a heart MRI scan at baseline or within a few weeks of this baseline visit, and at

6 months. Within these visits we will also perform blood tests (on the same day as the MRI scan) other non-invasive tests such as monitoring their heart rate, rhythm, and level of activity with patch accelerometers.

What are the possible benefits and risks of participating?
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 dilated cardiomyopathy (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.
Risks associated with taking a sample of blood from your arm include pain, bruising, light-headedness and on rare occasions, infection. The wearable devices will be a heart monitor patch attached to your upper chest. It should not cause you any harm or discomfort. 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 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. 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.

Where is the study run from?
Newcastle upon Tyne Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
February 2024 to December 2025

Who is funding the study?
AstraZeneca (UK)

Who is the main contact?
v.jeyalan@nhs.net

Contact information

Type(s)
Scientific

Contact name
Dr Visvesh Jeyalan

ORCID ID
https://orcid.org/0000-0003-3197-3764

Contact details
18 Cornel Road
Newcastle Upon Tyne
United Kingdom

NE7 7PT
+447423594609
v.jeyalan@nhs.net

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
334984

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 60481, IRAS 334984

Study information

Scientific Title
An observational study to correlate IMMUNE cell biology with Dilated CardioMyopathy patient characteristics (IMMUNE-DCM)

Acronym
IMMUNE-DCM

Study objectives
The evidence base and existing literature suggests that upregulation of CX3CR1, migration of immune cells, together with (cytomegalovirus) CMV seropositivity is associated with worse outcomes in patients with dilated cardiomyopathy. We hypothesise that this potentially occurs through cardiac inflammation and fibrosis resulting in adverse remodel-ling. Immune modulators to target this pathway may potentially improve outcomes above and beyond current guideline recommended therapy.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 13/02/2024, Wales REC 7 (Castlebridge 4, 15-19 Cowbridge Rd E, Cardiff, CF11 9AB, United Kingdom; +44 29 2023 0457; Wales.REC7@wales.nhs.uk), ref: 24/WA/0021

Study design
Observational cohort study

Primary study design
Observational

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Heart failure

Interventions
If the participant consents, a series of screening and baseline assessments will be conducted and recorded. These include capturing data from routine care on medical history, physical examinations, and previous cardiac imaging that the patient will have had performed.

The site principal investigator or designee will then evaluate the participant's eligibility based on these assessments at this point. If eligible, participants will then undergo the basic assessments including blood pressure assessment, a 12-lead electrocardiogram (ECG), as well as a quality-of-life questionnaire specific to heart failure. Participants will be provided with a heart monitoring device (a patch applied to the chest area) for a baseline assessment. A one minute sit-to-stand test will be performed with the device on, and the device will be worn for a duration of up to 7 days. The participants will be asked to return it, which may be via post, or a courier service may be arranged for collection. An MRI scan will be arranged (on the same day if possible), or on another date within 6 weeks of baseline.

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. We will use a contrast agent to enhance the images of blood flow to the heart. Patients will undergo the MRI scan following a (routine) MRI safety checklist screening procedure.

On the same day as the MRI, patients will also undergo blood tests to assess their routine bloods, inflammation markers, markers of heart failure, immune cells as well as bloods for a genetic assessment. The MRI and a number of blood tests will also be repeated at a 6-month visit. At each visit the participant will be asked about their current health status, medications, any hospitalisations, adverse events and other procedures they might have undergone since their last visit, additionally they will be asked to complete the same questionnaires.

All patients will be asked to consent for longer term follow up at 12 months from baseline, which would be subject to further funding. At 12 months, patients may be contacted and or medical records to assess for any clinical complications since their previous visit, specifically, hospitalisations with heart failure, any cardiac-related admissions and deaths regardless of cause.

Intervention Type
Other

Phase
Not Specified

Primary outcome(s)
1. CD3+CX3CR1+effector memory T-lymphocytes, measured by flow cytometry, at baseline and 6 months
2. Cardiac MRI parameters: T1 mapping, T2 mapping, ECV to assess inflammation and fibrosis. LV ejection fraction to assess left ventricular function and late gadolinium enhancement to assess for replacement fibrosis assessed at baseline

3. CMV seropositivity is measured by CMV IgG and IgM at baseline
4. Total T-cells and their main subsets (CD3, CD4 and CD8), Assessed by measured by the flow cytometry, at baseline and 6 months
5. Clonal CHIP mutation assessed at baseline with blood EDTA
6. Patch accelerometer to assess level of physical activity attached for up to 7 days at baseline and 6 months
7. Sit to stand test and the modified Borg scale to assess breathlessness at baseline and 6 months
8. KCCQ-23 score to assess quality of life at baseline and 6 months.

Key secondary outcome(s))
There are no secondary outcome measures

Completion date
31/12/2025

Eligibility

Key inclusion criteria
1. Established diagnosis of non-ischemic (dilated) cardiomyopathy, who have been receiving guideline-directed standard of care (SoC) pharmacological treatment for at least 3 months.
2. Diagnosis according to ESC guidelines: left ventricular or biventricular systolic dysfunction and dilatation that are not explained by abnormal loading conditions or coronary artery disease. Specifically - Systolic dysfunction defined by abnormal LV ejection fraction, measured using any modality and shown either by two independent imaging modalities or on two distinct occasions by the same technique, preferably echocardiography or CMR.
3. Ability to adhere to study requirements including provision of consent to genetic testing
4. Aged > = 18 years

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Heart failure due to either congenital heart disease, hypertensive heart disease, primary valvular heart disease, active acute myocarditis, hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy, restrictive cardiomyopathy or a known correctable metabolic cause;
2. Active vasculitis

3. Known cognitive impairment or unable to provide consent.
4. Serious co-existing medical condition, including but not limited to known hepatic failure, known renal failure with known eGFR < 30 mL/min/1.73m², or severe psychiatric disorder, known at the time of inclusion.
5. Cardiogenic shock, non-compensated acute heart failure and/or pulmonary oedema.
6. Cardiac resynchronization pacemaker implantation within previous 3 months.
7. Active infection at the time of enrolment.
8. History of established coronary disease with known epicardial stenosis of more than 70%
9. Patients unable to tolerate or undergo MRI scanning including patients with claustrophobia, cardiac pacemaker/defibrillator, ferromagnetic metal implants unless approved for use in MRI scanners or excessive body weight (BMI> 45 kg/m²)
10. Known allergy to gadolinium contrast.
11. Known planned hospitalisations (e.g. elective surgery), or other scheduled treatment for pre-existing conditions during the course of the study that could interfere with clinical assessment.
12. Any known previous diagnosis of invasive cancer within the last 5 years except for treated basal cell carcinoma of the skin.
13. Known pre-existing severe liver disease, including chronic hepatitis or alcohol-dependent liver cirrhosis
14. Other medical or social reasons for exclusion at the discretion of the investigator
15. Hypersensitivity to materials included in the patch.
16. Treatment with an investigational drug or other intervention assessment of which has not completed the primary endpoint or that clinically interferes with the present study endpoints will be excluded from this study.

Date of first enrolment
01/05/2024

Date of final enrolment
31/10/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
The Newcastle upon Tyne Hospitals NHS Foundation Trust
Freeman Hospital
Freeman Road
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN

Study participating centre

South Tees Hospitals NHS Foundation Trust
James Cook University Hospital
Marton Road
Middlesbrough
United Kingdom
TS4 3BW

Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Industry

Funder Name
AstraZeneca

Alternative Name(s)
AstraZeneca PLC, Pearl Therapeutics, AZ

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
All data generated or analysed during this study will be included in the subsequent results publication

IPD sharing plan summary

Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.1	31/01/2024	01/05/2024	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version 1.2	25/04/2025	01/05/2024	No	No