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Investigation of whether a drug called azacitidine can be safely used to make patients with hypertrophic cardiomyopathy feel better

Submission date 13/09/2025	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 15/12/2025	**Overall study status** Ongoing	
Last Edited 15/12/2025	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims
Hypertrophic cardiomyopathy is an inherited condition that affects the heart's ability to pump blood around the body. It affects around 1 in 500 people in the UK and can lead to heart failure. For people with hypertrophic cardiomyopathy everyday tasks like walking upstairs or to the shops becomes impossible. New drugs are needed to improve the lives of people with hypertrophic cardiomyopathy to stop the disease getting worse.
In support of this, we have discovered that a process called DNA methylation, which affects how your genetic code is expressed, can change in people with heart failure and other forms of heart disease. Pre-clinical studies have shown that changes in DNA methylation in diseased hearts are reversible using low doses of a drug called azacitidine, which also improves how the heart functions.
This drug is used in other types of patients with certain cancers but has not been used before to treat hypertrophic cardiomyopathy. The aim of this project is to test the drug in hypertrophic cardiomyopathy patients for the first time, through testing a range of low doses and to select a dose to study in more detail to provide evidence on how well it works to improve patient and heart health. The long-term benefits of this research could lead to the development of a new drug type for hypertrophic cardiomyopathy.

Who can participate?
Patients aged 18 to 75 years with non-obstructive hypertrophic cardiomyopathy (nHCM)

What does the study involve?
The study will involve receiving injections of the drug twice weekly for 16 weeks, blood samples will be taken as well as some physical exams including an echocardiogram and cardiac MRI. It will take 3 years to complete, although each participant will only be involved for the 16 weeks of treatment with a 4-week follow-up.

What are the possible benefits and risks of participating?
Although this study drug is already in common use for other conditions, it is possible participants will experience unwanted or unexpected side effects related to the medication. Any side effect

is recorded at each visit and will be tracked throughout the study. The doses administered in this trial will be much less than those given currently to cancer patients and therefore it is expected there will be less side effects at this dose. Nonetheless, intensive monitoring during the treatment period has been planned to minimise risk.
Some individuals may present with an allergy to the drug, these patients will be immediately taken off the drug and any symptoms will be treated accordingly. Participants will be monitored for at least 30 minutes after receiving each dose of the drug to check for any reactions such as allergy. The drug can also cause nausea and vomiting, as such anti-sickness drugs will be available for prescription to any participant who experiences this side effect. There can also be slight local reactions in the skin around the injection site such as inflammation or a rash. Injection sites will be reviewed at each site visit which will be twice-weekly and any required treatments such as antihistamines will be prescribed as required.
The greatest risk with this medication is a fall in blood counts which is why so many blood samples are required. Patients will have bloods checked before receiving any dose of the medication to make sure they are safe to begin treatment. Once treatment has started blood samples will be taken weekly and reviewed before the next week's treatment can be given to ensure it is safe for participants to continue taking the medication. As well as checking for blood counts, the blood samples will be used to monitor the health of the participants kidneys to ensure the drug is not effecting kidney function.
There are no adequate data on the use of the drug in pregnant women, therefore the potential risk for humans is unknown. Because of this, patients who are pregnant or breastfeeding will be excluded from the study and any participants are asked to use contraception throughout the study. Female participants of reproductive age will also have regular urine pregnancy tests to monitor them, if they become pregnant they will not receive anymore medication.
There is a significant time requirement from the participants in terms of having to attend the clinic twice-weekly for treatment for 16 weeks and also requiring an additional follow-up visit. Participants will be made aware of the commitment at the time of recruitment and will be reimbursed for travel and food expenses to help compensate for the efforts made by the participants.
All these risks are clearly outlined in the participant information sheet and during recruitment potential participants will have all risks clearly explained to them and be given time to discuss any concerns with the research team.

Where is the study run from?
Belfast City Hospital (UK)

When is the study starting and how long is it expected to run for?
September 2025 to January 2028

Who is funding the study?
1. British Heart Foundation (BHF)
2. Innovate UK
3. Heart Trust Fund

Who is the main contact?
1. Lana Dixon, lana.dixon@qub.ac.uk
2. Chris Watson, chris.watson@qub.ac.uk

Contact information

Type(s)

Scientific, Principal investigator

Contact name
Dr Lana Dixon

Contact details
274 Grosvenor Road
Belfast
United Kingdom
BT12 6BA
+44 (0)7710740876
lana.dixon@belfasttrust.hscni.net

Type(s)
Scientific

Contact name
Dr Chris Watson

ORCID ID
https://orcid.org/0000-0001-8749-0732

Contact details
Wellcome-Wolfson Institute for Experimental Medicine
Queen's University Belfast
97 Lisburn Road
Belfast
United Kingdom
BT9 7BL
+44 (0)2890 976478
chris.watson@qub.ac.uk

Additional identifiers

Integrated Research Application System (IRAS)
1009388

Protocol serial number
24078LD-UC

Study information

Scientific Title
A trial to evaluate the safety and efficacy of treatment with azacitadine in patients with symptomatic non-obstructive hypertrophic cardiomyopathy

Acronym
AZTEC

Study objectives

The aim of this study is to conduct an exploratory Phase II clinical trial to evaluate the safety and efficacy of azacitidine in patients with symptomatic non-obstructive hypertrophic cardiomyopathy (nHCM).

To explore the efficacy of 16 weeks treatment with azacitidine in HCM.

Ethics approval required
Ethics approval required

Ethics approval(s)
notYetSubmitted

Study design
Open randomized controlled trial

Primary study design
Interventional

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Hypertrophic cardiomyopathy (HCM)

Interventions
Phase 2a participants will all receive azacitidine treatment, with the dose being escalated /deescalated based on the TITE-CRM DLT model. During Phase 2b participants will be randomly assigned by 1:1 allocation to either azacitidine treatment arm or usual care/best available treatment (BAT).

Treatment arm:
Treatment arm refers to any participants receiving the study intervention, azacitidine. This includes all participants in Phase 2a but only those allocated to the study intervention in Phase 2b.
During Phase 2a participants will be allocated to receive either 5, 10, 15, 20, 25 or 30 mg/m2 dose of azacitidine, dependent on the dose escalation/de-escalation plan and recommendations from the DMEC based on the previous dose cohort.
Treatment with azacitidine will be administered on a bi-weekly basis for 16 weeks.
During Phase 2b participants allocated to treatment arm will receive the DMEC recommended and TMG approved dose of azacitidine as established during Phase 2a of the study. Treatment with azacitidine will be administered on a bi-weekly basis for 16 weeks.
To promote patient retention and follow-up visits will be consolidated where possible and adequate compensation sought to reimburse costs for travel expenses.

Usual care/best available treatment (BAT):
Usual care/BAT in symptomatic nHCM is the empirical management of patient's symptoms and complications they may develop over time. In the absence of randomised clinical trials pharmacological therapy is administered on an empirical basis to improve functional capacity and symptoms.

As a comparative group for this study participants allocated to usual care/BAT arm will be reviewed on a monthly basis. Visits will be consolidated where possible and use of “remote” consultations where in person visits or data are not required will be used in order to promote participant retention and follow-up.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Azacitidine

Primary outcome(s)
Phase 2a:
Safety of azacitidine, as defined by the incidence of dose-limiting toxicity (DLT) in each cohort. Adverse events will be monitored on days 8, 15, 22, 29, 43, 57, 71, 85, 99, 113 and at follow up on day 141.

Phase 2b:
Peak oxygen consumption (pVO2) measured by CPET at baseline (day 0) and following 16 weeks treatment (day 141).

Key secondary outcome(s))
All measured at baseline (day 0) and at 16 weeks (day 113):

Phase 2a:
1. The optimal dose of azacitidine for use in Phase 2b of the clinical trial
2. Patient functional class measured using the New York Heart Association functional classification of heart failure (NYHA) at baseline and following 16 weeks treatment with azacitidine
3. Quality of life measured using the Kansas City Cardiomyopathy Questionnaire (KCCQ) quality of life assessment tool at baseline and following 16 weeks treatment with azacitidine
4. Blood biomarkers including cardiac Troponin T and NT-proBNP measured using laboratory analysis at baseline and following 16 weeks treatment with azacitidine
5. Exercise tolerance measured by 6-minute walk test from baseline to week 16
6. Peak oxygen consumption (pVO2) measured by cardiopulmonary exercise testing (CPET) from baseline to week 16
7. Echocardiographic parameters of left ventricular function measured at baseline and following 16 weeks treatment with azacitidine
8. Cardiac MRI parameters of left ventricular function and late gadolinium enhancement measured at baseline and following 16 weeks treatment with azacitidine

Phase 2b:
1. Patient functional class measured using NYHA symptom class at baseline and following 16 weeks treatment with azacitidine
2. Quality of life measured using the Kansas City Cardiomyopathy Questionnaire (KCCQ) quality of life assessment tool at baseline and following 16 weeks treatment with azacitidine)
3. Blood biomarkers including cTnT and NT-proBNP measured using laboratory analysis at

baseline and following treatment with azacitidine
4. Exercise tolerance measured by 6-minute walk test at baseline and following 16 weeks treatment with azacitidine
5. Echocardiographic imaging parameters including systolic and diastolic function and global longitudinal strain measured at baseline and following 16 weeks treatment with azacitidine
6. Cardiac MRI parameters including systolic and diastolic function and late gadolinium enhancement at baseline and following 16 weeks treatment with azacitidine

Completion date
31/01/2028

Eligibility

Key inclusion criteria
1. Age 18 to 75 years who have a diagnosis of phenotype positive nHCM consistent with current American and European guidelines; Left ventricle (LV) wall thickness ≥15 mm (or ≥13 mm with a family history of HCM).
2. Symptomatic of nHCM at screening (defined as being NYHA functional class II/III).
3. Elevated N-terminal pro-hormone of Brain Natriuretic Peptide (NT pro-BNP) level >125 pg/ml as measured within 6 months of screening.
4. Left ventricular ejection fraction (LVEF) ≥55%.
5. Left Ventricular Outflow Tract (LVOT) peak gradient at rest and during Valsalva <50mmHg as determined by the echocardiography laboratory.
6. Men who are sexually active, must agree to acceptable birth control methods whilst receiving the the study drug and until 3 months after the last dose of study drug.
7. Women of childbearing potential, must agree to acceptable birth control methods during the study and until 6 months after the last dose of study drug.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
75 years

Sex
All

Total final enrolment
0

Key exclusion criteria

1. Presence of any active malignancy that required treatment within the last year
2. Patient is known to be pregnant or lactating
3. Consent to participate is declined
4. Absolute contraindication to study drug
5. NYHA functional class IV
6. Patients with reduced baseline blood counts (i.e. WBC <3.0 × 109/L or ANC <1.5 × 109/L or platelets <75.0 × 109/L) prior to the first treatment
7. Patient is enrolled in another investigational drug study within the past 6 months
8. Patient is incapable of completing exercise stress test

Date of first enrolment
01/02/2026

Date of final enrolment
01/12/2026

Locations

Countries of recruitment
United Kingdom

Northern Ireland

Study participating centre
Belfast City Hospital
51 Lisburn Rd
Belfast
Northern Ireland
BT9 7AB

Sponsor information

Organisation
Belfast Health and Social Care Trust

ROR
https://ror.org/02tdmfk69

Funder(s)

Funder type
Charity

Funder Name
British Heart Foundation

Alternative Name(s)
the_bhf, The British Heart Foundation, BHF

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Funder Name
Innovate UK

Alternative Name(s)
UK Research and Innovation Innovate UK, innovateuk

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Heart Trust Fund

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will be available upon request following the publication of the primary and secondary outcomes. Formal requests for data should be made in writing to Dr Lana Dixon (Chief Investigator) via the Northern Ireland Clinical Trials Unit (the trial co-ordinating centre) at AZTEC@nictu.hscni.net Requests will be reviewed on a case-by-case basis in collaboration with the Sponsor.

The study will comply with the good practice principles for sharing individual participant data from publicly funded clinical trials and data sharing will be undertaken in accordance with the

required regulatory requirements. Following the publication of the primary and secondary outcomes, any requests for data will need to be made in writing to the Chief investigator via the CTU, who will liaise with the Sponsor and obtain approval for the release of the data.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes