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

Submission date
22/01/2026

Recruitment status
Recruiting

Registration date
03/02/2026

Overall study status
Ongoing

Last Edited
29/04/2026

Condition category
Circulatory System

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Hypertrophic cardiomyopathy (HCM) is the most common inherited cardiac disorder, affecting 1 in 500 individuals in the general adult population. HCM is typically divided into two broad categories: obstructive hypertrophic cardiomyopathy (oHCM) and non-obstructive hypertrophic cardiomyopathy (nHCM). There has been a lot of advancement in treatment for oHCM; however, current treatment for nHCM focuses on relieving symptoms rather than treating the disease itself.
Azacitidine is an approved drug for the treatment of blood cancers, including myelodysplastic syndrome (MDS) and acute myeloid leukaemia (AML). Azacitidine has been shown to help improve markers of cardiac disease and could potentially protect against further damage to the heart. The AZTEC trial will investigate the safety and efficacy of azacitidine in patients with symptomatic nHCM. The study will be conducted in two stages: Phase IIa and Phase IIb.

Who can participate?
Adults aged 18-75 years who have a diagnosis of phenotype-positive HCM and are symptomatic of HSCN at screening, defined as being NYHA functional class II/III

What does the study involve?
Phase IIa is an initial dose-finding trial to find the best dose of azacitidine to use in the second part of the trial. Participants will be recruited in cohorts of 3 and treated with different doses of azacitidine, starting at a low dose and either increasing or decreasing the dose depending on how well the first cohort tolerated the treatment. Participants will receive twice-weekly injections of azacitidine for 16 weeks. This phase will recruit up to 24 participants and will determine the dose to be used in Phase IIb. Participants will undergo assessments, including a 6-minute walk test, echocardiogram and cardiac MRI before and after treatment to determine if treatment with azacitidine has changed these markers of cardiac health. They will also be asked

to complete a questionnaire before and after treatment that specifically asks questions around symptoms of cardiac disease, and will also have blood taken regularly to monitor their health throughout the treatment.

Phase IIb is a randomised trial where participants will be randomised 1:1 to receive either treatment (twice-weekly injections of azacitidine for 16 weeks) or remain on standard care. This phase will recruit up to 48 participants. Participants randomised to treatment will undergo the same process as Phase IIa with assessments before and after. Participants randomised to standard care will continue with their normal treatment plan but will be reviewed on specific days throughout the trial, which will involve having a physical exam and blood samples taken. They will also receive the assessments to assess cardiac health changes in the timeframe but without azacitidine treatment.

What are the possible benefits and risks of participating?
New research is vital to developing new treatments for diseases, especially for hypertrophic cardiomyopathy, which has limited treatment options available. However, as this is a new treatment we cannot be certain of the outcome and participants may experience side effects such as increased risk of infection and inflammation, risk of bleeding, allergic reaction, decreased appetite, insomnia, dizziness, headaches, fluid build up around the heart, changes to blood pressure, breathlessness, gastrointestinal upset (constipation, diarrhoea and vomiting), kidney and liver function impairment, muscle aches and spasms, skin irritation and general symptoms such as fever, fatigue and injection site discomfort. These events will be collected as safety outcomes, and any adverse effects will be monitored.

Where is the study run from?
The Northern Ireland Inherited Cardiac Conditions Services, Level 10 of the Belfast City Hospital (UK)

When is the study starting and how long is it expected to run for?
March 2026 to December 2028

Who is funding the study?
The British Heart Foundation and the Heart Trust Fund (UK)

Who is the main contact?
1. Dr Lana Dixon, lana.dixon@belfasttrust.hscni.net
2. Dr Megan Campbell, AZTEC@nictu.hscni.net

Contact information

Type(s)
Public

Contact name
Dr Megan Campbell

Contact details
7 Lennoxvale
Belfast
United Kingdom
BT9 5BY

+44 (0)28961 51447
AZTEC@nictu.hscni.net

Type(s)
Principal investigator

Contact name
Dr Lana Dixon

Contact details
274 Grosvenor Road
Belfast
United Kingdom
BT12 6AB
+44 (0)7557 507523
Lana.dixon@qub.ac.uk

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
97 Lisburn Road
Queen's University Belfast
Belfast
United Kingdom
BT9 7BL
+44 (0)2890 976478
chris.watson@qub.ac.uk

Additional identifiers

Integrated Research Application System (IRAS)
1009388

Study information

Scientific Title
AZacitidine Treatment Effect on hypertrophic Cardiomyopathy: an open-label dose escalation Phase IIa trial followed by a randomised, controlled, open-label Phase IIb efficacy trial

Acronym
AZTEC

Study objectives
Phase IIa Primary Objective:
1. To assess the safety of 16 weeks treatment with azacitidine in patients with symptomatic nHCM.

Phase IIa Secondary Objectives:
1. To determine the optimal dose of azacitidine for use in Phase 2b of the study.
2. To gather efficacy data on 16 weeks treatment with azacitidine in patients with symptomatic nHCM

Phase IIb Primary Objective:
1. To evaluate the efficacy of 16 weeks treatment with azacitidine in patients with symptomatic nHCM using pV02 as measured by CPET.

Phase IIb Secondary Objective:
1. Evaluation of the effects of 16 weeks treatment with azacitidine on other important cardiopulmonary outcomes.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 28/11/2025, North East - Tyne and Wear South Research Ethics Committee (NHSBT Newcastle Blood Donor Centre Holland Drive, Newcastle upon Tyne, NE2 4NQ, United Kingdom; +44 (0)207 104 8000; tyneandwearsouth.rec@hra.nhs.uk), ref: 25/NE/0191

Primary study design
Interventional

Allocation
Non-randomized controlled trial

Masking
Open (masking not used)

Control
Active

Assignment
Parallel

Purpose
Treatment

Study type(s)

Health condition(s) or problem(s) studied
Symptomatic non-obstructive hypertrophic cardiomyopathy (nHCM)

Interventions

The investigational medicinal product (IMP) will be azacitidine. Azacitidine is an epigenetic-modifying therapy that irreversibly binds to DNA methyltransferases, thus inhibiting their enzymatic activity.

Phase IIa is an open-label dose escalation/de-escalation trial in which cohorts of study subjects are planned to receive varying doses of azacitidine. Up to 24 subjects will be recruited during this phase and treated in dose cohorts (n = 3). The drug will be administered by twice-weekly subcutaneous injection in dose cohorts (n = 3) for 16 weeks.

Phase IIb is an open-label randomised controlled efficacy trial. This 12-month Phase IIb trial will recruit 48 participants who will be randomly assigned in a 1:1 ratio using randomly permuted block randomisation to either azacitidine treatment or usual care/best available treatment (BAT). Participants within the treatment arm will receive twice weekly injection of azacitidine for 16 weeks. The dose administered will be based on the recommendation made upon completion of the Phase IIa trial.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome(s)
1. Safety of azacitidine measured using the incidence of dose limiting toxicity (DLT) in each cohort. at twice-weekly from consent until last injection (day 0-113) and again at final check up on day 141

Key secondary outcome(s)
1. The optimal dose of azacitidine for use in Phase IIb of the study measured using safety outcome and dose finding in Phase IIa at completion of Phase IIa

2. Functional classification of heart failure measured using New York Heart Association (NYHA) classification at baseline and following 16 weeks treatment

3. Quality of life measured using Kansas City Cardiomyopathy Questionnaire (KCCQ) at baseline and following 16 weeks treatment

4. Blood biomarkers measured using Cardiac Troponin T and NT-proBNP at baseline and following 16 weeks treatment

5. Exercise tolerance measured using 6-minute walk test at baseline and following 16 weeks treatment

6. Exercise tolerance: peak oxygen consumption (pV02) measured using cardiopulmonary Exercise Testing (CPET) at baseline and following 16 weeks treatment

7. Echocardiographic imaging parameters including systolic and diastolic function and global longitudinal strain measured using echocardiogram at baseline and following 16 weeks treatment

8. Cardiac MRI parameters including systolic and diastolic function, left ventricular hypertrophy and late gadolinium enhancement, measured using cardiac MRI at baseline and following 16 weeks treatment

Completion date
29/12/2028

Eligibility

Key inclusion criteria
1. Age 18 to 75 years who have a diagnosis of phenotype-positive HCM 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 HCM at screening (defined as being NYHA functional class II/III).
3. Elevated N-terminal pro-hormone of Brain Natriuretic Peptide (NT-proBNP) 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 <50 mmHg as determined by echocardiography.
6. Total bilirubin ≤1.5 × ULN (≤ 2.0 × ULN in patients with known Gilbert's syndrome) with direct bilirubin ≤1 × ULN.
7. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤2.5 × ULN.
8. Estimated glomerular filtration rate (eGFR, CKD-EPI) >30 ml/min/1.73m2 at screening.

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. Patient has a history of malignancy in the last 5 years (with the exception of non-melanoma skin cancer).
2. Patient is known to be pregnant or lactating.

3. Absolute contraindication to study drug.
4. Patients with reduced baseline blood counts (i.e. White Blood Cells (WBC) <3.0 × 10e9/L or Absolute Neutrophil Counts (ANC) <1.5 × 10e9/L or platelets <75.0 × 10e9/L) prior to the first treatment.
5. Participation in a clinical study involving any other investigational medication in the 12 weeks or 5 half-lives (whichever is longer) of the medication before recruitment, unless it can be documented that the participant was in a placebo treatment arm.
6. Patient is not capable of performing cardiopulmonary exercise stress test.
7. Men who are sexually active, who have not agreed to acceptable birth control methods whilst receiving study drug and until 3 months after the last dose of study drug.
8. Women of childbearing potential, who have not agreed to acceptable birth control methods whilst receiving study drug and until 6 months after the last dose of study drug.
9. Patients with uncontrolled cardiovascular disease, including unstable angina, uncontrolled hypertension, and NYHA class IV heart failure.
10. Known HIV, HBV, or HCV infection.
11. Type 1 diabetes or uncontrolled or unstable Type 2 diabetes, with a HbA1C of >75mmol/mol.
12. Patient has not recovered from an infection that required systemic treatment.
13. Consent to participate is declined.

Date of first enrolment
30/06/2026

Date of final enrolment
28/04/2028

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

Funder Name
British Heart Foundation

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

Funding Body Type
Private sector organisation

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

Location
United Kingdom

Funder Name
Heart Trust Fund

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available