ISRCTN18530525 https://doi.org/10.1186/ISRCTN18530525

# Copper (II) chelation therapy in the treatment of hypertrophic cardiomyopathy (HCM)

| Submission date | Recruitment status | [_] Prospectively registered |
|---|---|---|
| 08/01/2015 | No longer recruiting | [_] Protocol |
| **Registration date** | **Overall study status** | [_] Statistical analysis plan |
| 09/01/2015 | Completed | [X] Results |
| **Last Edited** | **Condition category** | [_] Individual participant data |
| 04/11/2020 | Circulatory System | |

**Plain English summary of protocol**

Background and study aims
Hypertrophic cardiomyopathy (HCM) is the most common inherited heart condition. One in every 500 people have the condition and there are one million sufferers in Europe. It is a disorder of the heart muscle (myocardium) itself results in
heart muscle thickening (hypertrophy) and scarring (fibrosis). This condition can cause disturbances in heart rhythms which can cause sudden death, indeed HCM is the leading cause of sudden death in young (<35 years old) people. HCM hearts process energy inefficiently, and progressive heart failure can also develop. There are currently no treatments that alter the natural history of the disease. It is not clear how the faulty gene causes the muscle to become thickened, however current research suggests that it is a problem with our body cells not being able to use energy properly. Trientine is a medication used to treat Wilson disease, a rare disorder which leads to excess copper accumulation and tissue damage since 1969. It also acts on energy usage to improve it. Trientine has been found to reduce heart muscle hypertrophy in patients with diabetes. The aim of this study is to investigate whether Trientine will reduce the thickening of the heart in HCM patients, improve its energy efficiency and therefore represent the first disease modifying therapy in HCM.

Who can participate?
Adults (aged at least 18) with HCM

What does the study involve?
Partipicants are randomly allocated into one of two groups. Those in group 1 receive their usual care. Those in group 2 are given trientine for 6 months. All patients undergo cardiac magnetic resonance (CMR) imaging at the start of the study and then after 6 months of therapy. CMR assesses how the heart uses its energy, myocardial hypertrophy and fibrosis.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
Wythenshawe Hospital (UK)

When is the study starting and how long is it expected to run for?
October 2014 to October 2015

Who is funding the study?
Medical Research Council (UK)

Who is the main contact?
Dr Anna Reid

# Contact information

### Type(s)
Scientific

### Contact name
Dr Anna Reid

### Contact details
Wythenshawe Hospital
Southmoor Road
Wythenshawe
Manchester
United Kingdom
M23 9LT

# Additional identifiers

### Protocol serial number
17776

# Study information

### Scientific Title
Copper chelation in hypertrophic cardiomyopathy: open-label pilot study of trientine in patients with hypertrophic cardiomyopathy

### Study objectives
Trientine will lead to left ventricular mass regression in hypertrophic cardiomyopathy, and improvement in myocardial energetics is associated with, or causative of, this LV regression.

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
NRES Committee North West- Liverpool East, 26/06/2014, ref: 14/NW/1015

### Primary study design
Interventional

### Study design
Non-randomised; Interventional

### Study type(s)
Treatment

### Health condition(s) or problem(s) studied
Topic: Cardiovascular disease; Subtopic: Cardiovascular (all Subtopics); Disease: Cardiovascular

### Interventions
Using trientine to assess if it improves fitness and heart function to improve treatment options for HCM. Participants will receive trientine for 6 months.

### Intervention Type
Drug

### Phase
Not Applicable

### Drug/device/biological/vaccine name(s)
Trientine

### Primary outcome(s)
Myocardial energetics, measured using cardiac MRI prior to starting treatment and at the end of treatment

### Key secondary outcome(s)
N/A

### Completion date
01/10/2015

## Eligibility

### Key inclusion criteria
1. Male or female > 18 years of age
2. Females will be non-pregnant and non-lactating with no intention of pregnancy during study treatment (see point 6)
3. Confirmed diagnosis of HCM in line with 2011 ACCF / AHA consensus document
4. Positive genotype
5. LV ejection fraction = 50%
6. Women of childbearing potential (not >1 year post-menopausal) must agree to use one of the following acceptable birth control methods:
6.1. True complete abstinence when this is in line with the preferred and usual lifestyle of the subject
6.2. Surgical sterilization of either the female subject in study (e.g., bilateral tubal ligation) or of her male partner (vasectomy with documented azoospermia) if he is the sole partner of that subject
6.3. Established progesterone-only hormonal contraception (implantable, patch, oral or intramuscular [IM]) administered for at least one month prior to study medication administration

6.4. Double barrier method: condom and occlusive cap (diaphragm) with spermicidal foam/gel /film/ cream/suppository

## Participant type(s)
Patient

## Healthy volunteers allowed
No

## Age group
Adult

## Lower age limit
18 Years

## Sex
All

## Total final enrolment
20

## Key exclusion criteria
1. History of any other cardiovascular disorder, including aortic stenosis, aortic coarctation, hypertension, renal artery stenosis, atrial fibrillation
2. NYHA Class III/IV heart failure
3. Diabetes mellitus
4. Contraindication to magnetic resonance imaging (MRI) scanning (including claustrophobia)
5. Known hypersensitivity to Trientine or excipients
6. Known hypersensitivity to Gadolinium-based contrast agent
7. eGFR < 50ml/min/1.73m2
8. BMI > 40kg/m2
9. History of significant malabsorption
10. Copper deficiency at baseline
11. Iron deficiency at baseline
12. Haemoglobin < 10g/dL
13. Unresolved haematological disorder
14. Severe hepatic impairment
15. Untreated thyroid disease
16. Autoimmune disorders/connective tissue disease
17. Drug or alcohol abuse
18. Pregnancy/breast-feeding. Women of childbearing potential (not >2 years post- menopausal and/or not surgically sterilised) must have a negative blood serum pregnancy test, performed at visit 1 prior to administration of study medication
19. Any clinically significant or unstable medical or psychiatric condition that would interfere with the patient’s ability to participate in the study
20. Any other condition, which in the opinion of the research team, may put participants at risk during the study, or which may affect the outcome of the study
21. New medication within the preceding month of the study (excluding short term prescriptions)
22. Participation in another study involving an investigational product in the previous 12 weeks

**Date of first enrolment**
06/01/2015

**Date of final enrolment**
01/10/2015

# Locations

**Countries of recruitment**
United Kingdom

England

**Study participating centre**
**Wythenshawe Hospital**
Southmoor Road
Wythenshawe
Manchester
United Kingdom
M23 9LT

# Sponsor information

**Organisation**
University Hospital of South Manchester NHS Foundation Trust

**ROR**
https://ror.org/00he80998

# Funder(s)

**Funder type**
Government

**Funder Name**
Medical Research Council

**Alternative Name(s)**
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

**Funding Body Type**

Government organisation

**Funding Body Subtype**
National government

**Location**
United Kingdom

# Results and Publications

## Individual participant data (IPD) sharing plan

### IPD sharing plan summary
Not provided at time of registration

### Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Results article | results | 01/08/2017 | 04/11/2020 | Yes | No |