

**Clinical trial results:****Copper Chelation in Hypertrophic Cardiomyopathy: Open-label pilot study of Trientine in patients with hypertrophic cardiomyopathy****Summary**

EudraCT number	2014-001577-13
Trial protocol	GB
Global end of trial date	02 September 2016

Results information

Result version number	v1 (current)
This version publication date	04 June 2020
First version publication date	04 June 2020

Trial information**Trial identification**

Sponsor protocol code	CC-HCM-01
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	U1111-1155-6428
Other trial identifiers	REC reference: 14/NW/1015

Notes:

Sponsors

Sponsor organisation name	Manchester University NHS Foundation Trust
Sponsor organisation address	29 Grafton Street, Manchester, United Kingdom, M13 9WU
Public contact	Dr Lynne Webster, Head of the Research Office , Manchester University NHS Foundation Trust, +44 161 276 4125, research.sponsor@mft.nhs.uk
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Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 September 2016
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	02 September 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

i. Does Trientine lead to an improvement in high-energy phosphate metabolism (myocardial energetics, i.e. energy processing) in patients with HCM?

Protection of trial subjects:

Patients may develop adverse effects whilst taking Trientine. These risks will be fully explained to patients before they decide to participate in the trial. After patients have completed this clinical study, Trientine will be discontinued. Although Trientine is a licensed medication, it may not be possible to prescribe it "offlabel", even if some of the patients have benefited from it. This will be made clear to patients before they enrol in the trial. MRI scanning is a standard clinical imaging modality in every day clinical use and risks to study participants from MRI scanning are very small, provided they do not have any contraindications to MRI scanning (patients with contraindications to MRI scanning will be excluded). Echocardiography is a standard clinical imaging modality in every day clinical use.

Background therapy:

N/A

Evidence for comparator:

There is no comparator in this trial.

Actual start date of recruitment	10 October 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 22
Worldwide total number of subjects	22
EEA total number of subjects	22

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0

Adolescents (12-17 years)	0
Adults (18-64 years)	18
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment to the trial opened on 10/10/2014 following R&D approval and sponsor green light. A total of 23 participants were recruited to the trial but four withdrew prior to completion.

Pre-assignment

Screening details:

Inclusion criteria:

- Male or female > 18 years of age
- Females will be non-pregnant and non-lactating with no intention of pregnancy during study treatment*
- Confirmed diagnosis of HCM in line with 2011 ACCF / AHA consensus document
- Positive genotype
- LV ejection fraction \geq 50%

Period 1

Period 1 title	Trintine (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

N/A - there is no placebo or active comparator so there is no blinding in this trial.

Arms

Arm title	Trintine tablets
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Arm description:

Patients will be supplied with Trintine tablets. The starting dose prescribed will be 600mg per day (taken as 300mg twice daily) for the first week, followed by 1200mg/day (taken as 600mg twice daily) thereafter under the direction of a medical doctor. The study doctor will contact each patient after 1 week to ensure they feel well enough to continue, and if they do, to remind them to increase their dose.

Arm type	Experimental
Investigational medicinal product name	Trintine dihydrochloride
Investigational medicinal product code	SUB04953MIG
Other name	PL 41626/0001
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Trintine dihydrochloride is a divalent copper selective chelator. It forms a stable complex with divalent copper. This complex is readily excreted by the kidney, increasing copper excretion. It also reduces intestinal absorption. Patients will be supplied with Trintine tablets. The starting dose prescribed will be 600mg per day (taken as 300mg twice daily) for the first week, followed by 1200mg/day (taken as 600mg twice daily) thereafter under the direction of a medical doctor. The study doctor will contact each patient after 1 week to ensure they feel well enough to continue, and if they do, to remind them to increase their dose.

Number of subjects in period 1	Trientine tablets
Started	22
Visit 1 - Baseline assessment	20
Visit 2 - Supply of Trientine tablets	20
Visit 3 - 1 month after IMP initiation	17
Visit 4 - 3 months after IMP initiation	16
Visit 5 - 5 months after IMP initiation	15
Visit 6 - 6 months after IMP initiation	15
Completed	15
Not completed	7
Change of personal circumstance	1
Adverse event, non-fatal	4
Ineligible for participation	2

Baseline characteristics

Reporting groups

Reporting group title	Trientine
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Reporting group description: -

Reporting group values	Trientine	Total	
Number of subjects	22	22	
Age categorical			
Units: Subjects			
Adults (18-64 years)	18	18	
From 65-84 years	4	4	
Age continuous			
Units: years			
arithmetic mean	55.5		
standard deviation	± 8.4	-	
Gender categorical			
Units: Subjects			
Female	5	5	
Male	15	15	
Missing	2	2	
ACEi / ARB			
Units: Subjects			
Yes	1	1	
No	19	19	
Missing	2	2	
Beta-blockers			
Units: Subjects			
Yes	10	10	
No	10	10	
Missing	2	2	
Calcium Channel Blockers			
Units: Subjects			
Yes	1	1	
No	19	19	
Missing	2	2	
Spironolactone			
Units: Subjects			
Yes	0	0	
No	20	20	
Missing	2	2	
NYHA			
Units: Subjects			
NYHA I	14	14	
NYHA II	6	6	
Missing	2	2	

Body surface area Units: metres squared arithmetic mean standard deviation	2.06 ± 0.25	-	
Systolic Blood Pressure Units: mm/Hg arithmetic mean standard deviation	130 ± 15	-	
Diastolic Blood Pressure Units: mm/Hg arithmetic mean standard deviation	81 ± 12	-	
Heart rate Units: bpm arithmetic mean standard deviation	66.5 ± 16.3	-	
PCr/ATP ratio Units: ratio arithmetic mean standard deviation	1.27 ± 0.44	-	
EF Units: percentage arithmetic mean standard deviation	69.0 ± 6.8	-	
Mass/BSA Units: g/metres squared arithmetic mean standard deviation	73.5 ± 20.0	-	
Haemoglobin Units: g/l arithmetic mean standard deviation	145.5 ± 13.3	-	
Urea Units: mmol/l arithmetic mean standard deviation	5.1 ± 1.0	-	
Creatinine Units: µmol/l arithmetic mean standard deviation	75.0 ± 13.0	-	
eGFR Units: ml/min/1.73m squared arithmetic mean standard deviation	82.7 ± 8.6	-	
Alk. Phos Units: iu/l arithmetic mean standard deviation	73.0 ± 19.8	-	
ALT Units: iu/l arithmetic mean standard deviation	20.5 ± 6.4	-	

Magnesium Units: mmol/l arithmetic mean standard deviation	0.87 ± 0.08	-	
Serum Copper Units: µmol/l arithmetic mean standard deviation	16.5 ± 2.3	-	
Serum Caeruloplasmin Units: g/l arithmetic mean standard deviation	0.23 ± 0.03	-	
Serum Zinc Units: µmol/l arithmetic mean standard deviation	20.4 ± 5.4	-	
BSA Units: m squared arithmetic mean standard deviation	2.07 ± 0.28	-	
Exercise time Units: min arithmetic mean standard deviation	14.7 ± 3.2	-	
Anaerobic Threshold Units: l/mn arithmetic mean standard deviation	1.41 ± 0.46	-	
VO2 Max Units: l/mn arithmetic mean standard deviation	2.44 ± 0.81	-	
PR interval Units: ms arithmetic mean standard deviation	184 ± 20	-	
QRS duration Units: ms arithmetic mean standard deviation	110 ± 12	-	
QTc Units: ms arithmetic mean standard deviation	432 ± 27	-	
E velocity Units: cm/s arithmetic mean standard deviation	60.8 ± 16.7	-	
A velocity Units: cm/s arithmetic mean standard deviation	64.4 ± 23.0	-	

E/A ratio Units: ratio arithmetic mean standard deviation	1.11 ± 0.67	-	
Mean S* Velocity Units: cm/s arithmetic mean standard deviation	6.9 ± 2.5	-	
Mean E* Velocity Units: cm/s arithmetic mean standard deviation	6.8 ± 3.4	-	
Mean A* Velocity Units: cm/s arithmetic mean standard deviation	7.4 ± 3.1	-	
Mean E/E* Units: cm/s arithmetic mean standard deviation	10.7 ± 3.3	-	
Mitral Decel. Time Units: ms arithmetic mean standard deviation	295 ± 79	-	
LVEDV Units: ml arithmetic mean standard deviation	171 ± 36	-	
LVESV Units: ml arithmetic mean standard deviation	54 ± 20	-	
SV Units: ml arithmetic mean standard deviation	117 ± 22	-	
EF Units: percentage arithmetic mean standard deviation	69 ± 7	-	
LVM Units: grams arithmetic mean standard deviation	152 ± 54	-	
LVEDVi Units: ml/m squared arithmetic mean standard deviation	84 ± 10	-	
LVESVi Units: ml/m squared arithmetic mean standard deviation	26 ± 7	-	

SVi Units: ml/m squared arithmetic mean standard deviation	58 ± 9	-	
LVMi Units: g/m squared arithmetic mean standard deviation	73 ± 20	-	
Native septal T1 Units: ms arithmetic mean standard deviation	1060 ± 47	-	
ECV Fraction Units: percentage arithmetic mean standard deviation	30.0 ± 4.5	-	
Total Myocardial Volume Units: ml arithmetic mean standard deviation	145 ± 52	-	
ECM Volume Units: ml arithmetic mean standard deviation	44 ± 18	-	
Cellular Volume Units: ml arithmetic mean standard deviation	101 ± 36	-	
GLS Units: percentage arithmetic mean standard deviation	-18.3 ± 3.4	-	
LAESV Units: ml arithmetic mean standard deviation	75.8 ± 43.6	-	
LAEDV Units: ml arithmetic mean standard deviation	124.4 ± 51.3	-	
Pre-atrial contraction vol Units: ml arithmetic mean standard deviation	102.9 ± 46.7	-	
LAESVi Units: ml/m squared arithmetic mean standard deviation	37.3 ± 17.9	-	
LAEDVi Units: ml/m squared arithmetic mean standard deviation	61.7 ± 21.9	-	

Pre-atrial contraction vol i Units: ml/m squared arithmetic mean standard deviation	50.9 ± 19.8	-	
Total EF Units: percentage arithmetic mean standard deviation	41.3 ± 8.3	-	
Passive EF Units: percentage arithmetic mean standard deviation	18.0 ± 5.8	-	
Booster EF Units: percentage arithmetic mean standard deviation	28.4 ± 8.9	-	
LA Expansion Index Units: Index arithmetic mean standard deviation	0.73 ± 0.22	-	
Total strain Units: percentage arithmetic mean standard deviation	20.0 ± 3.9	-	
Peak systolic strain rate Units: -1 arithmetic mean standard deviation	0.75 ± 0.13	-	
Passive Strain Units: percentage arithmetic mean standard deviation	9.747 ± 3.06	-	
Peak early negative strain rate Units: -1 arithmetic mean standard deviation	-0.5 ± 0.29	-	
Active strain Units: percentage arithmetic mean standard deviation	10.53 ± 3.08	-	
Peak late negative strain rate Units: -1 arithmetic mean standard deviation	-0.68 ± 0.20	-	

End points

End points reporting groups

Reporting group title	Trientine tablets
Reporting group description: Patients will be supplied with Trientine tablets. The starting dose prescribed will be 600mg per day (taken as 300mg twice daily) for the first week, followed by 1200mg/day (taken as 600mg twice daily) thereafter under the direction of a medical doctor. The study doctor will contact each patient after 1 week to ensure they feel well enough to continue, and if they do, to remind them to increase their dose.	

Primary: LVM

End point title	LVM ^[1]
End point description:	
End point type	Primary
End point timeframe: Visit 6	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: This is a pilot trial with no comparator group. Results are given as descriptive statistics only with comparisons to baseline (p=0.06).

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: grams				
arithmetic mean (standard deviation)	147 (± 55)			

Statistical analyses

No statistical analyses for this end point

Primary: Native septal T1

End point title	Native septal T1 ^[2]
End point description:	
End point type	Primary
End point timeframe: Visit 6	

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: This is a pilot trial with no comparator group. Results are given as descriptive statistics only with comparisons to baseline (p=0.06).

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: ms				
arithmetic mean (standard deviation)	1049 (± 42)			

Statistical analyses

No statistical analyses for this end point

Primary: ECV Fraction

End point title	ECV Fraction ^[3]
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End point description:

End point type	Primary
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End point timeframe:

Visit 6

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: This is a pilot trial with no comparator group. Results are given as descriptive statistics only with comparisons to baseline (p=0.06).

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: percentage				
arithmetic mean (standard deviation)	29.5 (± 4.0)			

Statistical analyses

No statistical analyses for this end point

Primary: PCr/ATP Ratio

End point title	PCr/ATP Ratio ^[4]
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End point description:

End point type	Primary
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End point timeframe:

Visit 6

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: This is a pilot trial with no comparator group. Results are given as descriptive statistics only with comparisons to baseline (p=0.46).

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: Ratio				
arithmetic mean (standard deviation)	1.4 (\pm 0.39)			

Statistical analyses

No statistical analyses for this end point

Secondary: Haemoglobin

End point title	Haemoglobin
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: g/L				
arithmetic mean (standard deviation)	143.2 (\pm 12.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Urea

End point title	Urea
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: mmol/l				
arithmetic mean (standard deviation)	4.9 (± 1.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Creatinine

End point title	Creatinine
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: µmol/L				
arithmetic mean (standard deviation)	74.2 (± 11.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: eGFR

End point title	eGFR
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: ml/min/1.73m squared				
arithmetic mean (standard deviation)	84.5 (± 7.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Alk Phos

End point title	Alk Phos
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: iu/l				
arithmetic mean (standard deviation)	78.6 (± 19.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: ALT

End point title	ALT
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: IU/L				
arithmetic mean (standard deviation)	23.6 (± 5.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Magnesium

End point title	Magnesium
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: mmol/l				
arithmetic mean (standard deviation)	0.81 (± 0.12)			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Copper

End point title	Serum Copper
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: $\mu\text{mol/l}$				
arithmetic mean (standard deviation)	16.6 (\pm 2.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Caeruloplasmin

End point title	Serum Caeruloplasmin
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: g/L				
arithmetic mean (standard deviation)	0.24 (\pm 0.03)			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Zinc

End point title	Serum Zinc
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: µmol/l				
arithmetic mean (standard deviation)	25.3 (± 7.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Systolic BP

End point title	Systolic BP
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: mmHg				
arithmetic mean (standard deviation)	125 (± 15)			

Statistical analyses

No statistical analyses for this end point

Secondary: Diastolic BP

End point title	Diastolic BP
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: mmHg				
arithmetic mean (standard deviation)	74 (\pm 7)			

Statistical analyses

No statistical analyses for this end point

Secondary: BSA

End point title	BSA
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: m squared				
arithmetic mean (standard deviation)	2.06 (\pm 0.28)			

Statistical analyses

No statistical analyses for this end point

Secondary: E velocity

End point title	E velocity
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: cm/s				
arithmetic mean (standard deviation)	61.8 (± 12.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: A velocity

End point title	A velocity
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: cm/s				
arithmetic mean (standard deviation)	63.7 (± 20.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: E/A ratio

End point title	E/A ratio
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: ratio				
arithmetic mean (standard deviation)	1.10 (\pm 0.50)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean S* Velocity

End point title	Mean S* Velocity
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: cm/s				
arithmetic mean (standard deviation)	8.1 (\pm 1.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean E* Velocity

End point title	Mean E* Velocity
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: cm/s				
arithmetic mean (standard deviation)	7.0 (± 2.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean A* Velocity

End point title	Mean A* Velocity
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: cm/s				
arithmetic mean (standard deviation)	8.4 (± 2.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean E/E*

End point title	Mean E/E*
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: cm/s				
arithmetic mean (standard deviation)	10.1 (± 3.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mitral Decel. Time

End point title	Mitral Decel. Time
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: seconds				
arithmetic mean (standard deviation)	265 (± 47)			

Statistical analyses

No statistical analyses for this end point

Secondary: Exercise time

End point title	Exercise time
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: minutes				
arithmetic mean (standard deviation)	14.4 (± 2.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Anaerobic Threshold

End point title	Anaerobic Threshold
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: l/mn				
arithmetic mean (standard deviation)	1.47 (± 0.36)			

Statistical analyses

No statistical analyses for this end point

Secondary: VO2 Max

End point title	VO2 Max
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: l/mn				
arithmetic mean (standard deviation)	2.41 (\pm 0.74)			

Statistical analyses

No statistical analyses for this end point

Secondary: PR interval

End point title	PR interval
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: ms				
arithmetic mean (standard deviation)	182 (\pm 19)			

Statistical analyses

No statistical analyses for this end point

Secondary: QRS duration

End point title	QRS duration
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: ms				
arithmetic mean (standard deviation)	109 (± 13)			

Statistical analyses

No statistical analyses for this end point

Secondary: QTc

End point title	QTc
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: ms				
arithmetic mean (standard deviation)	429 (± 20)			

Statistical analyses

No statistical analyses for this end point

Secondary: Heart rate

End point title	Heart rate
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: bpm				
arithmetic mean (standard deviation)	58.8 (± 9.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: LVEDV

End point title	LVEDV
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: ml				
arithmetic mean (standard deviation)	169 (± 38)			

Statistical analyses

No statistical analyses for this end point

Secondary: LVESV

End point title	LVESV
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: ml				
arithmetic mean (standard deviation)	52 (\pm 20)			

Statistical analyses

No statistical analyses for this end point

Secondary: SV

End point title	SV
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: ml				
arithmetic mean (standard deviation)	117 (\pm 23)			

Statistical analyses

No statistical analyses for this end point

Secondary: LVEDVi

End point title	LVEDVi
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: ml/m squared				
arithmetic mean (standard deviation)	84 (± 12)			

Statistical analyses

No statistical analyses for this end point

Secondary: LVESVi

End point title	LVESVi
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: ml/m squared				
arithmetic mean (standard deviation)	26 (± 8)			

Statistical analyses

No statistical analyses for this end point

Secondary: SVi

End point title	SVi
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: ml/m squared				
arithmetic mean (standard deviation)	59 (\pm 8)			

Statistical analyses

No statistical analyses for this end point

Secondary: LVMI

End point title	LVMI
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: g/m squared				
arithmetic mean (standard deviation)	73 (\pm 22)			

Statistical analyses

No statistical analyses for this end point

Secondary: EF

End point title	EF
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: percentage				
arithmetic mean (standard deviation)	70 (± 6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Total Myocardial Volume

End point title	Total Myocardial Volume
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: ml				
arithmetic mean (standard deviation)	140 (± 53)			

Statistical analyses

No statistical analyses for this end point

Secondary: ECM Volume

End point title	ECM Volume
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: ml				
arithmetic mean (standard deviation)	42 (\pm 17)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cellular Volume

End point title	Cellular Volume
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: ml				
arithmetic mean (standard deviation)	99 (\pm 37)			

Statistical analyses

No statistical analyses for this end point

Secondary: GLS

End point title	GLS
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: percentage				
arithmetic mean (standard deviation)	-19.4 (± 3.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: LAESV

End point title	LAESV
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: ml				
arithmetic mean (standard deviation)	65.8 (± 40.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: LAEDV

End point title	LAEDV
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: ml				
arithmetic mean (standard deviation)	114.6 (± 47.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pre-atrial contraction vol

End point title	Pre-atrial contraction vol
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: ml				
arithmetic mean (standard deviation)	93.3 (± 40.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: LAESVi

End point title	LAESVi
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: ml/m squared				
arithmetic mean (standard deviation)	32.6 (± 17.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: LAEDVi

End point title	LAEDVi
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: ml/m squared				
arithmetic mean (standard deviation)	57.4 (± 20.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pre-atrial contraction vol i

End point title	Pre-atrial contraction vol i
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: ml/m squared				
arithmetic mean (standard deviation)	46.6 (± 17.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Total EP

End point title	Total EP
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: percentage				
arithmetic mean (standard deviation)	45.5 (± 12.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Passive EF

End point title	Passive EF
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: percentage				
arithmetic mean (standard deviation)	18.7 (± 4.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Booster EF

End point title	Booster EF
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: percentage				
arithmetic mean (standard deviation)	33.2 (± 13.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: LA Expansion Index

End point title	LA Expansion Index
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: Index				
arithmetic mean (standard deviation)	0.94 (\pm 0.54)			

Statistical analyses

No statistical analyses for this end point

Secondary: Total strain

End point title	Total strain
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: percentage				
arithmetic mean (standard deviation)	21.5 (\pm 5.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Peak systolic strain rate

End point title	Peak systolic strain rate
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: -1				
arithmetic mean (standard deviation)	0.83 (± 0.19)			

Statistical analyses

No statistical analyses for this end point

Secondary: Passive Strain

End point title	Passive Strain
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: percentage				
arithmetic mean (standard deviation)	11.1 (± 5.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Peak early negative strain rate

End point title	Peak early negative strain rate
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: -1				
arithmetic mean (standard deviation)	-0.49 (\pm 0.23)			

Statistical analyses

No statistical analyses for this end point

Secondary: Active Strain

End point title	Active Strain
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: percentage				
arithmetic mean (standard deviation)	10.41 (\pm 4.20)			

Statistical analyses

No statistical analyses for this end point

Secondary: Peak late negative strain rate

End point title	Peak late negative strain rate
End point description:	
End point type	Secondary
End point timeframe:	
Visit 6	

End point values	Trientine tablets			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: -1				
arithmetic mean (standard deviation)	-0.66 (± 0.30)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events assessed by the study investigators were recorded and followed up until resolution.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	1
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Reporting groups

Reporting group title	Trintine tablets
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Reporting group description:

Patients will be supplied with Trintine tablets. The starting dose prescribed will be 600mg per day (taken as 300mg twice daily) for the first week, followed by 1200mg/day (taken as 600mg twice daily) thereafter under the direction of a medical doctor. The study doctor will contact each patient after 1 week to ensure they feel well enough to continue, and if they do, to remind them to increase their dose.

Serious adverse events	Trintine tablets		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 22 (13.64%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Wrist Sprain			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Palpitations requiring admission			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Appendicitis			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Trientine tablets		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 22 (95.45%)		
General disorders and administration site conditions			
Dizziness			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Increased exercise capacity			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Headache			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Adhesive capsulitis of the shoulder			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Immune system disorders			
Common Cold			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Gastrointestinal disorders			
Gastric complaints			
subjects affected / exposed	5 / 22 (22.73%)		
occurrences (all)	5		
Increased Urinary Frequency			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Chest infection			

subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 3		
Psychiatric disorders Vivid dreams subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2		
Infections and infestations Influenza-like illness subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 February 2015	Substantial amendment 1: - Addition of St Mary's Hospital, CMFT as a PIC site. - Addition of instructions for use of the cool bag system. The amendment received REC favourable opinion 23/03/2015.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None.

Notes: