

**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 |
|-----------------------|-----------|

**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 |
| Scientific contact           | Anna Reid, Manchester University NHS Foundation Trust, +44 7743647285, Anna.Reid@MFT.NHS.UK                                               |

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 |
|-----------|------------------|

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.

| <b>Number of subjects in period 1</b>   | 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 |
|-----------------------|-----------|

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

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

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

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

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

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                   |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                     | Trientine tablets |
| Reporting group description:<br>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 <sup>[1]</sup> |
| End point description:          |                    |
| End point type                  | Primary            |
| End point timeframe:<br>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).

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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 <sup>[2]</sup> |
| End point description:          |                                 |
| End point type                  | Primary                         |
| End point timeframe:<br>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).

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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 <sup>[3]</sup> |
|-----------------|-----------------------------|

End point description:

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

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).

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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 <sup>[4]</sup> |
|-----------------|------------------------------|

End point description:

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

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).

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |             |

|                                      |                     |  |  |  |
|--------------------------------------|---------------------|--|--|--|
| <b>End point values</b>              | 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                |           |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |            |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |           |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |           |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |           |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |           |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |              |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |                      |

|                                      |                    |  |  |  |
|--------------------------------------|--------------------|--|--|--|
| <b>End point values</b>              | 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                |            |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |             |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |              |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |           |

|                                      |                    |  |  |  |
|--------------------------------------|--------------------|--|--|--|
| <b>End point values</b>              | 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                |            |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |            |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |           |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | Trientine tablets |  |  |  |
| Subject group type                   | Reporting group   |  |  |  |
| Number of subjects analysed          | 15                |  |  |  |
| Units: ratio                         |                   |  |  |  |
| arithmetic mean (standard deviation) | 1.10 (± 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                |                  |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | Trientine tablets |  |  |  |
| Subject group type                   | Reporting group   |  |  |  |
| Number of subjects analysed          | 15                |  |  |  |
| Units: cm/s                          |                   |  |  |  |
| arithmetic mean (standard deviation) | 8.1 (± 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                |                  |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | Trientine tablets |  |  |  |
| Subject group type                   | Reporting group   |  |  |  |
| Number of subjects analysed          | 15                |  |  |  |
| Units: cm/s                          |                   |  |  |  |
| arithmetic mean (standard deviation) | 7.0 ( $\pm$ 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                |                  |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | Trientine tablets |  |  |  |
| Subject group type                   | Reporting group   |  |  |  |
| Number of subjects analysed          | 15                |  |  |  |
| Units: cm/s                          |                   |  |  |  |
| arithmetic mean (standard deviation) | 8.4 ( $\pm$ 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                |           |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |                    |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |               |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |                     |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |           |

|                                      |                    |  |  |  |
|--------------------------------------|--------------------|--|--|--|
| <b>End point values</b>              | 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                |             |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |              |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | Trientine tablets |  |  |  |
| Subject group type                   | Reporting group   |  |  |  |
| Number of subjects analysed          | 15                |  |  |  |
| Units: ms                            |                   |  |  |  |
| arithmetic mean (standard deviation) | 109 ( $\pm$ 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                |           |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | Trientine tablets |  |  |  |
| Subject group type                   | Reporting group   |  |  |  |
| Number of subjects analysed          | 15                |  |  |  |
| Units: ms                            |                   |  |  |  |
| arithmetic mean (standard deviation) | 429 ( $\pm$ 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                |            |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |           |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |           |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | Trientine tablets |  |  |  |
| Subject group type                   | Reporting group   |  |  |  |
| Number of subjects analysed          | 15                |  |  |  |
| Units: ml                            |                   |  |  |  |
| arithmetic mean (standard deviation) | 52 (± 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                |           |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | Trientine tablets |  |  |  |
| Subject group type                   | Reporting group   |  |  |  |
| Number of subjects analysed          | 15                |  |  |  |
| Units: ml                            |                   |  |  |  |
| arithmetic mean (standard deviation) | 117 (± 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                |           |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | Trientine tablets |  |  |  |
| Subject group type                   | Reporting group   |  |  |  |
| Number of subjects analysed          | 15                |  |  |  |
| Units: ml/m squared                  |                   |  |  |  |
| arithmetic mean (standard deviation) | 84 ( $\pm$ 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                |           |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | Trientine tablets |  |  |  |
| Subject group type                   | Reporting group   |  |  |  |
| Number of subjects analysed          | 15                |  |  |  |
| Units: ml/m squared                  |                   |  |  |  |
| arithmetic mean (standard deviation) | 26 ( $\pm$ 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                |           |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | Trientine tablets |  |  |  |
| Subject group type                   | Reporting group   |  |  |  |
| Number of subjects analysed          | 15                |  |  |  |
| Units: ml/m squared                  |                   |  |  |  |
| arithmetic mean (standard deviation) | 59 (± 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                |           |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | Trientine tablets |  |  |  |
| Subject group type                   | Reporting group   |  |  |  |
| Number of subjects analysed          | 15                |  |  |  |
| Units: g/m squared                   |                   |  |  |  |
| arithmetic mean (standard deviation) | 73 (± 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                |           |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |                         |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |            |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | Trientine tablets |  |  |  |
| Subject group type                   | Reporting group   |  |  |  |
| Number of subjects analysed          | 15                |  |  |  |
| Units: ml                            |                   |  |  |  |
| arithmetic mean (standard deviation) | 42 (± 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                |                 |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | Trientine tablets |  |  |  |
| Subject group type                   | Reporting group   |  |  |  |
| Number of subjects analysed          | 15                |  |  |  |
| Units: ml                            |                   |  |  |  |
| arithmetic mean (standard deviation) | 99 (± 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                |           |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |           |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |           |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |                            |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |           |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |           |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |                              |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |           |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |            |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |            |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |                    |

|                                      |                    |  |  |  |
|--------------------------------------|--------------------|--|--|--|
| <b>End point values</b>              | 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

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |                |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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                |                                 |

|                                      |                     |  |  |  |
|--------------------------------------|---------------------|--|--|--|
| <b>End point values</b>              | 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                |               |

|                                      |                     |  |  |  |
|--------------------------------------|---------------------|--|--|--|
| <b>End point values</b>              | 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                |                                |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 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 |
|-----------------|----------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |   |
|--------------------|---|
| Dictionary version | 1 |
|--------------------|---|

### 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.

| Serious adverse events                            | Trientine 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 %

| <b>Non-serious adverse events</b>                     | 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<br>occurrences (all)                                                          | 3 / 22 (13.64%)<br>3 |  |  |
| Psychiatric disorders<br>Vivid dreams<br>subjects affected / exposed<br>occurrences (all)                 | 2 / 22 (9.09%)<br>2  |  |  |
| Infections and infestations<br>Influenza-like illness<br>subjects affected / exposed<br>occurrences (all) | 1 / 22 (4.55%)<br>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:<br>- Addition of St Mary's Hospital, CMFT as a PIC site.<br>- Addition of instructions for use of the cool bag system.<br>The amendment received REC favourable opinion 23/03/2015. |

Notes:

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### 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: