



## Clinical trial results:

### Perhexiline therapy in patients with heart failure with preserved left ventricular ejection fraction(HFpEF syndrome)

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2006-001109-28   |
| Trial protocol           | GB               |
| Global end of trial date | 03 February 2014 |

#### Results information

|                                |                |
|--------------------------------|----------------|
| Result version number          | v1 (current)   |
| This version publication date  | 18 August 2018 |
| First version publication date | 18 August 2018 |

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | pgrf/141/09 |
|-----------------------|-------------|

##### Additional study identifiers

|                                    |                |
|------------------------------------|----------------|
| ISRCTN number                      | ISRCTN25678870 |
| ClinicalTrials.gov id (NCT number) | NCT00839228    |
| WHO universal trial number (UTN)   | -              |

Notes:

#### Sponsors

|                              |                                                                                        |
|------------------------------|----------------------------------------------------------------------------------------|
| Sponsor organisation name    | University of Aberdeen                                                                 |
| Sponsor organisation address | Research Governance, Foresterhill House Annexe, Aberdeen, United Kingdom, AB25 2ZB     |
| Public contact               | Michael P Frenneaux, University of Aberdeen, 0121 4146926, M.P.Frenneaux@bham.ac.uk    |
| Scientific contact           | Michael P Frenneaux, University of Aberdeen, 0121 4146926, M.P.Frenneaux@bham.ac.uk    |
| Sponsor organisation name    | NHS Grampian                                                                           |
| Sponsor organisation address | R&D Office, Foresterhill House Annexe, Aberdeen, United Kingdom, AB25 2ZB              |
| Public contact               | Professor Frenneaux, NHS Grampian Health Board, 0121 4146926, M.P.Frenneaux@bham.ac.uk |
| Scientific contact           | Professor Frenneaux, NHS Grampian Health Board, 0121 4146926, M.P.Frenneaux@bham.ac.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                       | 01 August 2014   |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 03 February 2014 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 03 February 2014 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

To test whether perhexiline improve exercise capacity (peak vo2) in patients with heart failure with preserved left ventricular ejection fraction(HFpEFsyndrome)

Protection of trial subjects:

A total of 72 patients who meet the selection criteria will be recruited from NHS Grampian and University Hospitals Birmingham NHS trust. Informed consent will be obtained from each patient.

Background therapy:

We postulate that perhexiline-induced shifts in metabolism will lead to improved cardiac energetic, exercise capacity, quality of life and myocardial function in HFpEF patients.

Evidence for comparator: -

|                                                           |              |
|-----------------------------------------------------------|--------------|
| Actual start date of recruitment                          | 01 July 2011 |
| Long term follow-up planned                               | No           |
| Independent data monitoring committee (IDMC) involvement? | Yes          |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United Kingdom: 72 |
| Worldwide total number of subjects   | 72                 |
| EEA total number of subjects         | 72                 |

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)                      | 19 |

|                     |    |
|---------------------|----|
| From 65 to 84 years | 51 |
| 85 years and over   | 2  |

## Subject disposition

### Recruitment

Recruitment details:

A total of 72 patients who meet the selection criteria will be recruited from NHS Grampian and University Hospitals Birmingham NHS trust.

### Pre-assignment

Screening details:

Clinical symptoms and signs consistent with HF; LVEF >50%, with no evidence of significant valvular disease, no hypertrophic cardiomyopathy and no evidence of pericardial constriction; A peak VO<sub>2</sub> <80% predicted, with RER >1 and with a pattern of gas exchange on metabolic exercise testing indicating a cardiac cause for limitation; All patient recrui

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall trial (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Randomised - controlled        |
| Blinding used                | Double blind                   |
| Roles blinded                | Subject, Investigator, Carer   |

### Arms

|                  |                        |
|------------------|------------------------|
| <b>Arm title</b> | Perhexiline vs Placebo |
|------------------|------------------------|

Arm description:

Perhexiline 100mg o bd for 3 months

|                                        |                     |
|----------------------------------------|---------------------|
| Arm type                               | Active comparator   |
| Investigational medicinal product name | Perhexiline Maleate |
| Investigational medicinal product code | 021418              |
| Other name                             | PEXSIG              |
| Pharmaceutical forms                   | Tablet              |
| Routes of administration               | Oral use            |

Dosage and administration details:

Diameter 8.5mm. Each tablet contains 100mg Perhexiline Maleate (100mg o bd 3 months)

| Number of subjects in period 1 | Perhexiline vs Placebo |
|--------------------------------|------------------------|
| Started                        | 72                     |
| Completed                      | 72                     |

## Baseline characteristics

### Reporting groups

Reporting group title

Overall trial

Reporting group description: -

| Reporting group values                                | Overall trial | Total |  |
|-------------------------------------------------------|---------------|-------|--|
| Number of subjects                                    | 72            | 72    |  |
| Age categorical                                       |               |       |  |
| Units: Subjects                                       |               |       |  |
| In utero                                              | 0             | 0     |  |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0             | 0     |  |
| Newborns (0-27 days)                                  | 0             | 0     |  |
| Infants and toddlers (28 days-23<br>months)           | 0             | 0     |  |
| Children (2-11 years)                                 | 0             | 0     |  |
| Adolescents (12-17 years)                             | 0             | 0     |  |
| Adults (18-64 years)                                  | 19            | 19    |  |
| From 65-84 years                                      | 51            | 51    |  |
| 85 years and over                                     | 2             | 2     |  |
| Gender categorical                                    |               |       |  |
| Units: Subjects                                       |               |       |  |
| Female                                                | 48            | 48    |  |
| Male                                                  | 24            | 24    |  |

## End points

### End points reporting groups

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | Perhexiline vs Placebo |
|-----------------------|------------------------|

Reporting group description:

Perhexiline 100mg o bd for 3 months

### Primary: Peak oxygen consumption (Vo2max)

|                 |                                                 |
|-----------------|-------------------------------------------------|
| End point title | Peak oxygen consumption (Vo2max) <sup>[1]</sup> |
|-----------------|-------------------------------------------------|

End point description:

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

End point timeframe:

Not documented.

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: No publication has been submitted to date therefore unable to specify statistical analysis.

| End point values                   | Perhexiline vs Placebo |  |  |  |
|------------------------------------|------------------------|--|--|--|
| Subject group type                 | Reporting group        |  |  |  |
| Number of subjects analysed        | 72                     |  |  |  |
| Units: carbon dioxide re-breathing |                        |  |  |  |
| number (not applicable)            | 72                     |  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All SAEs will be reported to the sponsor and PI within 1 working day of discovery or notification of the event. All AEs occurring during the study observed by the investigator or reported by the patient will be reported on the CRF.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                    |      |
|--------------------|------|
| Dictionary name    | None |
| Dictionary version | 0    |

### Reporting groups

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | Perhexiline vs Placebo |
|-----------------------|------------------------|

Reporting group description: -

| Serious adverse events                            | Perhexiline vs Placebo |  |  |
|---------------------------------------------------|------------------------|--|--|
| Total subjects affected by serious adverse events |                        |  |  |
| subjects affected / exposed                       | 3 / 5 (60.00%)         |  |  |
| number of deaths (all causes)                     | 0                      |  |  |
| number of deaths resulting from adverse events    | 0                      |  |  |
| Cardiac disorders                                 |                        |  |  |
| Musculoskeletal Chest Pain                        |                        |  |  |
| subjects affected / exposed                       | 1 / 5 (20.00%)         |  |  |
| occurrences causally related to treatment / all   | 1 / 1                  |  |  |
| deaths causally related to treatment / all        | 0 / 0                  |  |  |
| Blood and lymphatic system disorders              |                        |  |  |
| Pulmonary embolism                                |                        |  |  |
| subjects affected / exposed                       | 1 / 5 (20.00%)         |  |  |
| occurrences causally related to treatment / all   | 1 / 1                  |  |  |
| deaths causally related to treatment / all        | 0 / 0                  |  |  |
| Endocrine disorders                               |                        |  |  |
| Pancreatic cancer                                 |                        |  |  |
| subjects affected / exposed                       | 1 / 5 (20.00%)         |  |  |
| occurrences causally related to treatment / all   | 1 / 1                  |  |  |
| deaths causally related to treatment / all        | 0 / 0                  |  |  |

Frequency threshold for reporting non-serious adverse events: 5 %

| <b>Non-serious adverse events</b>                                                       | Perhexiline vs<br>Placebo |  |  |
|-----------------------------------------------------------------------------------------|---------------------------|--|--|
| Total subjects affected by non-serious<br>adverse events<br>subjects affected / exposed | 2 / 5 (40.00%)            |  |  |
| Surgical and medical procedures                                                         |                           |  |  |
| Knee Replacement<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 5 (20.00%)<br><br>1   |  |  |
| Spinal Surgery<br>subjects affected / exposed<br>occurrences (all)                      | 1 / 5 (20.00%)<br><br>1   |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date         | Amendment                                                   |
|--------------|-------------------------------------------------------------|
| 27 June 2012 | AM05 - Addition of BNP tests at baseline and post exercise. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported