



## Clinical trial results:

### Bone marrow-derived mesenchymal stromal cell treatment in patients with severe ischaemic heart failure: a randomized placebo-controlled trial (MSC-HF trial)

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2008-001850-42 |
| Trial protocol           | DK             |
| Global end of trial date | 31 July 2014   |

#### Results information

|                                   |  |
|-----------------------------------|--|
| Result version number             | v1 (current)   |
| This version publication date     | 07 April 2020  |
| First version publication date    | 07 April 2020  |
| Summary attachment (see zip file) | MSC CHF summary (Summary.docx)<br>Publication European Heart Journal (Mathiasen - MSC-HF EHJ 2015 published.pdf) |

#### Trial information

##### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | MSC-HF |
|-----------------------|--------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00644410 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Rigshospitalet   |
| Sponsor organisation address | Blegdamsvej 9, Copenhagen, Denmark, 2100   |
| Public contact               | Jens Kastrup Professor, Department of Cardiology 2014, +45 35452819, jens.kastrup@regionh.dk |
| Scientific contact           | Jens Kastrup Professor, Department of Cardiology 2014, +45 35452819, jens.kastrup@regionh.dk |

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                       | 30 November 2014 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 31 July 2014     |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 31 July 2014     |
| Was the trial ended prematurely?                     | No               |

Notes:

---

**General information about the trial**

---

Main objective of the trial:

It is a single centre, randomised controlled study of the effect of NOGA guided direct intramyocardial injection of mesenchymal stromal cells on the development of new myocardium and blood vessels in patients with heart failure.

Stem cells will be obtained from the bone marrow and culture expanded for 6 - 8 weeks before injected into the myocardium.

The patients will be followed for safety, clinical symptoms, MRI and CT for 12 months

Protection of trial subjects:

The GMP unit in the Capital Region of Denmark monitored the study.

Background therapy: -

Evidence for comparator: -

|   |                                       |
|---|---------------------------------------|
| Actual start date of recruitment                          | 21 April 2009                         |
| Long term follow-up planned                               | Yes                                   |
| Long term follow-up rationale                             | Efficacy, Safety, Scientific research |
| Long term follow-up duration                              | 1 Years                               |
| Independent data monitoring committee (IDMC) involvement? | No                                    |

Notes:

---

**Population of trial subjects**

---

**Subjects enrolled per country**

|                                      |             |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Denmark: 60 |
| Worldwide total number of subjects   | 60          |
| EEA total number of subjects         | 60          |

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) | 8  |
| From 65 to 84 years  | 52 |
| 85 years and over    | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Patients followed for Heart failure or referred for an invasive investigation to the Department of Cardiology was screened for participation in the study.

### Pre-assignment

Screening details:

At time of inclusion the patients were on maximum tolerable medication with no changes in medication for two months. Patients had LVEF $\leq$ 45% and were New York Heart Association (NYHA) Class II-III. Major exclusion criteria were acute coronary syndrome, stroke or transitional cerebral ischemia within six weeks, revascularization within 4 months, moder

### Pre-assignment period milestones

|                              |    |
|------------------------------|----|
| Number of subjects started   | 60 |
| Number of subjects completed | 60 |

### 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, Monitor, Data analyst, Carer, Assessor |

### Arms

|                              |              |
|------------------------------|--------------|
| Are arms mutually exclusive? | Yes          |
| <b>Arm title</b>             | Active - MSC |

Arm description:

Injection of autologous bone marrow derived mesenchymal stromal cells

|  |                           |
|--|---------------------------|
| Arm type                               | Active comparator         |
| Investigational medicinal product name | Mesenchymal stromal cells |
| Investigational medicinal product code |                           |
| Other name                             |                           |
| Pharmaceutical forms                   | Solution for injection    |
| Routes of administration               | Intracardiac use          |

Dosage and administration details:

The patient was treated with the number of cell produced after two cell culture expansion passages : mean of  $77.5 \pm 67.9 \times 10^6$  (inter quartile range  $53.8 \times 10^6$ ) MSCs

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

Arm description:

Saline injection

|  |                  |
|--|------------------|
| Arm type                               | Placebo          |
| Investigational medicinal product name | Saline           |
| Investigational medicinal product code |                  |
| Other name                             |                  |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Intracardiac use |

Dosage and administration details:

0.2 ml isotonic NaCl

| <b>Number of subjects in period 1</b> | Active - MSC | Placebo |
|---------------------------------------|--------------|---------|
| Started                               | 40           | 20      |
| Completed                             | 40           | 20      |

## Baseline characteristics

### Reporting groups

|   |              |
|---|--------------|
| Reporting group title   | Active - MSC |
| Reporting group description:<br>Injection of autologous bone marrow derived mesenchymal stromal cells |              |
| Reporting group title   | Placebo      |
| Reporting group description:<br>Saline injection  |              |

| Reporting group values             | Active - MSC | Placebo | Total |
|------------------------------------|--------------|---------|-------|
| Number of subjects                 | 40           | 20      | 60    |
| Age categorical<br>Units: Subjects |              |         |       |

|   |               |                |    |
|---|---------------|----------------|----|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 66.1<br>± 7.7 | 64.2<br>± 10.6 | -  |
| Gender categorical<br>Units: Subjects                                   |               |                |    |
| Female  | 4             | 6              | 10 |
| Male  | 36            | 14             | 50 |

## End points

### End points reporting groups

|   |              |
|---|--------------|
| Reporting group title   | Active - MSC |
| Reporting group description:<br>Injection of autologous bone marrow derived mesenchymal stromal cells |              |
| Reporting group title   | Placebo      |
| Reporting group description:<br>Saline injection  |              |

### Primary: Left ventricular end-systolic volume

|  |                                      |
|--|--------------------------------------|
| End point title  | Left ventricular end-systolic volume |
| End point description:                                 |                                      |
| End point type   | Primary                              |
| End point timeframe:<br>Baseline to 6 months follow-up |                                      |

| End point values                         | Active - MSC         | Placebo            |  |  |
|--|----------------------|--------------------|--|--|
| Subject group type                       | Reporting group      | Reporting group    |  |  |
| Number of subjects analysed              | 40                   | 20                 |  |  |
| Units: ml                                |                      |                    |  |  |
| geometric mean (confidence interval 95%) | -7.6 (-11.8 to -3.4) | 5.4 (-0.4 to 11.2) |  |  |

### Statistical analyses

|   |                        |
|---|------------------------|
| Statistical analysis title              | difference             |
| Comparison groups                       | Active - MSC v Placebo |
| Number of subjects included in analysis | 60                     |
| Analysis specification                  | Pre-specified          |
| Analysis type                           | equivalence            |
| P-value                                 | < 0.05                 |
| Method                                  | t-test, 2-sided        |

## Adverse events

### Adverse events information<sup>[1]</sup>

Timeframe for reporting adverse events:

baseline to 6 months follow-up

Adverse event reporting additional description:

There was no serious adverse event due to the mesenchymal stem cell therapy

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

### Dictionary used

|                 |                   |
|-----------------|-------------------|
| Dictionary name | Hospitals reports |
|-----------------|-------------------|

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

### Reporting groups

|                       |                          |
|-----------------------|--------------------------|
| Reporting group title | Mesenchymal stromal cell |
|-----------------------|--------------------------|

Reporting group description:

Patients treated with mesenchymal stromal cells

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Patients treated with placebo

| Serious adverse events                            | Mesenchymal stromal cell | Placebo        |  |
|---|--------------------------|----------------|--|
| Total subjects affected by serious adverse events |                          |                |  |
| subjects affected / exposed                       | 0 / 40 (0.00%)           | 0 / 20 (0.00%) |  |
| number of deaths (all causes)                     | 1                        | 1              |  |
| number of deaths resulting from adverse events    | 0                        | 0              |  |

Frequency threshold for reporting non-serious adverse events: 1 %

| Non-serious adverse events                            | Mesenchymal stromal cell | Placebo        |  |
|---|--------------------------|----------------|--|
| Total subjects affected by non-serious adverse events |                          |                |  |
| subjects affected / exposed                           | 0 / 40 (0.00%)           | 0 / 20 (0.00%) |  |

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: There were no adverse or serious adverse events that could be related to the treatment.



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

---

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

---

### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/25926562>