



## Clinical trial results:

**Pilot study investigating the effect of intra-coronary and intra-myocardial application of enriched CD133pos autologous bone marrow derived stem cells for improving left ventricular function in chronic ischemic cardiomyopathy**

### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2009-013103-63   |
| Trial protocol           | DE               |
| Global end of trial date | 02 November 2016 |

### Results information

|                                   |                                                                                                 |
|-----------------------------------|-------------------------------------------------------------------------------------------------|
| Result version number             | v1 (current)                                                                                    |
| This version publication date     | 09 October 2020                                                                                 |
| First version publication date    | 09 October 2020                                                                                 |
| Summary attachment (see zip file) | Final Report-2009-013103-63-#1884-AlsterMACS (2009-013103-63-#1884-AlsterMACS final report.doc) |

### Trial information

#### Trial identification

|                       |      |
|-----------------------|------|
| Sponsor protocol code | 1884 |
|-----------------------|------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01337011 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |                                                                                   |
|------------------------------|-----------------------------------------------------------------------------------|
| Sponsor organisation name    | Asklepios Kliniken Hamburg GmbH                                                   |
| Sponsor organisation address | Ruebenkamp 226, Hamburg, Germany, 22307                                           |
| Public contact               | Dr. Kai Jaquet, ASKLEPIOS proresearch, +49 040181885-3034, k.jaquet@asklepios.com |
| Scientific contact           | Dr. Kai Jaquet, ASKLEPIOS proresearch, +49 040181885-3034, k.jaquet@asklepios.com |

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:

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**Results analysis stage**

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|                                                      |                  |
|------------------------------------------------------|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 02 November 2016 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 02 November 2016 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 02 November 2016 |
| Was the trial ended prematurely?                     | Yes              |

Notes:

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**General information about the trial**

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Main objective of the trial:

To assess the safety, feasibility, and efficacy of intra-myocardial as well as intra-coronary CD133pos. BM cell therapy on left ventricular ejection fraction as measured by echocardiography.

Protection of trial subjects:

Whole intervention is done under sedation.

Background therapy:

Standard of care according to medical guidelines at that time

Evidence for comparator: -

|                                                           |                  |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment                          | 01 November 2011 |
| Long term follow-up planned                               | Yes              |
| Long term follow-up rationale                             | Safety, Efficacy |
| Long term follow-up duration                              | 12 Months        |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

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|                                      |             |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Germany: 10 |
| Worldwide total number of subjects   | 10          |
| EEA total number of subjects         | 10          |

Notes:

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**Subjects enrolled per age group**

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|                                           |   |
|-------------------------------------------|---|
| 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)                      | 9 |
| From 65 to 84 years                       | 1 |
| 85 years and over                         | 0 |

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## Subject disposition

### Recruitment

Recruitment details:

Recruitment of 6 patients in 2012 and 4 patients in 2013

### Pre-assignment

Screening details:

Patients with chronic heart disease

### Pre-assignment period milestones

|                              |    |
|------------------------------|----|
| Number of subjects started   | 10 |
| Number of subjects completed | 10 |

### Period 1

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

### Arms

|                              |                            |
|------------------------------|----------------------------|
| Are arms mutually exclusive? | Yes                        |
| <b>Arm title</b>             | intra-coronary application |

Arm description:

Intracoronary application of CD133pos. autologous bone marrow derived stem cells

|                                        |                                                     |
|----------------------------------------|-----------------------------------------------------|
| Arm type                               | Active comparator                                   |
| Investigational medicinal product name | CD133pos. autologous bone marrow derived stem cells |
| Investigational medicinal product code |                                                     |
| Other name                             | CD133pos. autologous bone marrow derived stem cells |
| Pharmaceutical forms                   | Concentrate for solution for infusion               |
| Routes of administration               | Intracardiac use                                    |

Dosage and administration details:

single dose

|                  |                         |
|------------------|-------------------------|
| <b>Arm title</b> | intra-myocardial CD133+ |
|------------------|-------------------------|

Arm description:

intra-myocardial application of CD133po. cells

|                                        |                                                     |
|----------------------------------------|-----------------------------------------------------|
| Arm type                               | Active comparator                                   |
| Investigational medicinal product name | CD133pos. autologous bone marrow derived stem cells |
| Investigational medicinal product code |                                                     |
| Other name                             | CD133+                                              |
| Pharmaceutical forms                   | Concentrate for solution for injection              |
| Routes of administration               | Intramuscular use                                   |

Dosage and administration details:

total number of transplanted CD133+ BMNC = approx. 0.7 - 1.0 Mill. cells per patient

| <b>Number of subjects in period 1</b> | intra-coronary<br>application | intra-myocardial<br>CD133+ |
|---------------------------------------|-------------------------------|----------------------------|
| Started                               | 8                             | 2                          |
| Completed                             | 8                             | 2                          |

## Baseline characteristics

### Reporting groups

|                                                                                  |                            |
|----------------------------------------------------------------------------------|----------------------------|
| Reporting group title                                                            | intra-coronary application |
| Reporting group description:                                                     |                            |
| Intracoronary application of CD133pos. autologous bone marrow derived stem cells |                            |
| Reporting group title                                                            | intra-myocardial CD133+    |
| Reporting group description:                                                     |                            |
| intra-myocardial application of CD133po. cells                                   |                            |

| Reporting group values                                                    | intra-coronary application | intra-myocardial CD133+ | Total |
|---------------------------------------------------------------------------|----------------------------|-------------------------|-------|
| Number of subjects                                                        | 8                          | 2                       | 10    |
| Age categorical                                                           |                            |                         |       |
| inclusion criterium age:<br>adults (18-64 years) and adults (65-84 years) |                            |                         |       |
| Units: Subjects                                                           |                            |                         |       |
| In utero                                                                  | 0                          | 0                       | 0     |
| Preterm newborn infants (gestational age < 37 wks)                        | 0                          | 0                       | 0     |
| Newborns (0-27 days)                                                      | 0                          | 0                       | 0     |
| Infants and toddlers (28 days-23 months)                                  | 0                          | 0                       | 0     |
| Children (2-11 years)                                                     | 0                          | 0                       | 0     |
| Adolescents (12-17 years)                                                 | 0                          | 0                       | 0     |
| Adults (18-64 years)                                                      | 8                          | 2                       | 10    |
| From 65-84 years                                                          | 0                          | 0                       | 0     |
| 85 years and over                                                         | 0                          | 0                       | 0     |
| Gender categorical                                                        |                            |                         |       |
| Units: Subjects                                                           |                            |                         |       |
| Female                                                                    | 0                          | 0                       | 0     |
| Male                                                                      | 8                          | 2                       | 10    |

### Subject analysis sets

|                                                                                                                                                                                                                                   |                                      |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|
| Subject analysis set title                                                                                                                                                                                                        | CD133+ intramyocardial+intracoronary |
| Subject analysis set type                                                                                                                                                                                                         | Per protocol                         |
| Subject analysis set description:                                                                                                                                                                                                 |                                      |
| Pilot study investigating the effect of intra-coronary and intra-myocardial application of enriched CD133pos autologous bone marrow derived stem cells for improving left ventricular function in chronic ischemic cardiomyopathy |                                      |

| Reporting group values                                                    | CD133+ intramyocardial+intracoronary |  |  |
|---------------------------------------------------------------------------|--------------------------------------|--|--|
| Number of subjects                                                        | 10                                   |  |  |
| Age categorical                                                           |                                      |  |  |
| inclusion criterium age:<br>adults (18-64 years) and adults (65-84 years) |                                      |  |  |
| Units: Subjects                                                           |                                      |  |  |
| In utero                                                                  | 0                                    |  |  |

|                                                       |    |  |  |
|-------------------------------------------------------|----|--|--|
| Preterm newborn infants<br>(gestational age < 37 wks) | 0  |  |  |
| Newborns (0-27 days)                                  | 0  |  |  |
| Infants and toddlers (28 days-23<br>months)           | 0  |  |  |
| Children (2-11 years)                                 | 0  |  |  |
| Adolescents (12-17 years)                             | 0  |  |  |
| Adults (18-64 years)                                  | 10 |  |  |
| From 65-84 years                                      | 0  |  |  |
| 85 years and over                                     | 0  |  |  |
| Gender categorical                                    |    |  |  |
| Units: Subjects                                       |    |  |  |
| Female                                                |    |  |  |
| Male                                                  |    |  |  |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                   |                                      |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|
| Reporting group title                                                                                                                                                                                                             | intra-coronary application           |
| Reporting group description:                                                                                                                                                                                                      |                                      |
| Intracoronary application of CD133pos. autologous bone marrow derived stem cells                                                                                                                                                  |                                      |
| Reporting group title                                                                                                                                                                                                             | intra-myocardial CD133+              |
| Reporting group description:                                                                                                                                                                                                      |                                      |
| intra-myocardial application of CD133po. cells                                                                                                                                                                                    |                                      |
| Subject analysis set title                                                                                                                                                                                                        | CD133+ intramyocardial+intracoronary |
| Subject analysis set type                                                                                                                                                                                                         | Per protocol                         |
| Subject analysis set description:                                                                                                                                                                                                 |                                      |
| Pilot study investigating the effect of intra-coronary and intra-myocardial application of enriched CD133pos autologous bone marrow derived stem cells for improving left ventricular function in chronic ischemic cardiomyopathy |                                      |

### Primary: safety

|                                                                  |         |
|------------------------------------------------------------------|---------|
| End point title                                                  | safety  |
| End point description:                                           |         |
| no pericardial effusion, no additional hospitalisation, no death |         |
| End point type                                                   | Primary |
| End point timeframe:                                             |         |
| 12 months                                                        |         |

| End point values            | intra-coronary application | intra-myocardial CD133+ | CD133+ intramyocardial+intracoronary |  |
|-----------------------------|----------------------------|-------------------------|--------------------------------------|--|
| Subject group type          | Reporting group            | Reporting group         | Subject analysis set                 |  |
| Number of subjects analysed | 8                          | 2                       | 10                                   |  |
| Units: hospitalisation      |                            |                         |                                      |  |
| number (not applicable)     | 0                          | 0                       | 0                                    |  |

### Statistical analyses

|                                                                                                                                 |                                                      |
|---------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------|
| Statistical analysis title                                                                                                      | paired t-test                                        |
| Statistical analysis description:                                                                                               |                                                      |
| Analysis of primary hypotheses:                                                                                                 |                                                      |
| The first primary hypothesis - change in ejection fraction between baseline vs. 6months – will be proved using a paired t-test. |                                                      |
| Comparison groups                                                                                                               | intra-coronary application v intra-myocardial CD133+ |
| Number of subjects included in analysis                                                                                         | 10                                                   |
| Analysis specification                                                                                                          | Post-hoc                                             |
| Analysis type                                                                                                                   | non-inferiority                                      |
| P-value                                                                                                                         | < 0.05                                               |
| Method                                                                                                                          | t-test, 2-sided                                      |
| Parameter estimate                                                                                                              | Mean difference (final values)                       |



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

12 months

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

|                 |                    |
|-----------------|--------------------|
| Dictionary name | ClinicalTrials.gov |
|-----------------|--------------------|

|                    |     |
|--------------------|-----|
| Dictionary version | PRV |
|--------------------|-----|

### Reporting groups

|                       |                                |
|-----------------------|--------------------------------|
| Reporting group title | cell therapy group (intra-myo) |
|-----------------------|--------------------------------|

Reporting group description:

Cell therapy group (intra-myocardial application of CD133+ BMNC)

|                       |                                 |
|-----------------------|---------------------------------|
| Reporting group title | cell therapy group (intra-coro) |
|-----------------------|---------------------------------|

Reporting group description:

cell therapy group (intra-coronary application of CD133+ BMNC)

| Serious adverse events                            | cell therapy group (intra-myo) | cell therapy group (intra-coro) |  |
|---------------------------------------------------|--------------------------------|---------------------------------|--|
| Total subjects affected by serious adverse events |                                |                                 |  |
| subjects affected / exposed                       | 0 / 8 (0.00%)                  | 0 / 2 (0.00%)                   |  |
| number of deaths (all causes)                     | 0                              | 0                               |  |
| number of deaths resulting from adverse events    | 0                              | 0                               |  |

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

| Non-serious adverse events                            | cell therapy group (intra-myo)                  | cell therapy group (intra-coro) |  |
|-------------------------------------------------------|-------------------------------------------------|---------------------------------|--|
| Total subjects affected by non-serious adverse events |                                                 |                                 |  |
| subjects affected / exposed                           | 2 / 8 (25.00%)                                  | 1 / 2 (50.00%)                  |  |
| Cardiac disorders                                     |                                                 |                                 |  |
| Ventricular arrhythmia                                | Additional description: ventricular tachycardia |                                 |  |
| subjects affected / exposed                           | 2 / 8 (25.00%)                                  | 1 / 2 (50.00%)                  |  |
| occurrences (all)                                     | 2                                               | 1                               |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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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.

|                                                                         |
|-------------------------------------------------------------------------|
| Due to financial problems and leaving of PI, study had to be cancelled. |
|-------------------------------------------------------------------------|

Notes: