



Clinical trial results:

INTRAMYOCARDIAL TRANSPLANTATION OF BONE MARROW STEM CELLS FOR IMPROVEMENT OF POST-INFARCT MYOCARDIAL REGENERATION IN ADDITION TO CABG SURGERY: a controlled prospective, randomized, double blinded multicenter trial

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2006-006404-11 |
| Trial protocol | DE |
| Global end of trial date | 04 September 2017 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 (current) |
| This version publication date | 26 August 2018 |
| First version publication date | 26 August 2018 |

Trial information

Trial identification

| | |
|-----------------------|------------------------|
| Sponsor protocol code | PERFECT001(M-2006-144) |
|-----------------------|------------------------|

Additional study identifiers

| | |
|------------------------------------|-----------------------------------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00950274 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | German Clinical Trials Register: DRKS00000213 |

Notes:

Sponsors

| | |
|------------------------------|-----------------------------------------------------------------------------|
| Sponsor organisation name | Miltenyi Biotec GmbH |
| Sponsor organisation address | Friedrich-Ebert-Straße 68, Bergisch Gladbach, Germany, 51429 |
| Public contact | Clinical Trials Information, Miltenyi Biotec GmbH, petrah@miltenyibiotec.de |
| Scientific contact | Clinical Trials Information, Miltenyi Biotec GmbH, petrah@miltenyibiotec.de |

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 | 04 September 2017 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|-------------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 04 September 2017 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

Determine whether injection of autologously derived bone marrow stem cells yielded a functional benefit in addition to the coronary artery bypass graft (CABG) operation as determined by left ventricular heart function (left ventricular ejection fraction [LVEF] determined with magnetic resonance imaging [MRI]).

Protection of trial subjects:

1. Recording of AEs
2. Assessment of Major adverse cardiovascular events (cardiac death, myocardial infarction, secondary intervention/reoperation, ventricular arrhythmia) and tachycardial supraventricular arrhythmia >160 bpm (Holter ECG).
3. Laboratory tests (post-operative check and specific tests for cell preparation)
4. Unwanted tissue changes (tumors) will be monitored by MRI and/or echocardiography
5. Vital signs (blood pressure and pulse)
6. Physical examination, 12-lead ECG

Background therapy: -

Evidence for comparator: -

| | |
|-----------------------------------------------------------|-----------------|
| Actual start date of recruitment | 01 October 2009 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 2 Years |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Germany: 82 |
| Worldwide total number of subjects | 82 |
| EEA total number of subjects | 82 |

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) | 46 |
| From 65 to 84 years | 36 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

| | |
|----------------------------|--------------------|
| Number of subjects started | 119 ^[1] |
|----------------------------|--------------------|

| | |
|------------------------------|----|
| Number of subjects completed | 82 |
|------------------------------|----|

Pre-assignment subject non-completion reasons

| | |
|----------------------------|---------------------------------|
| Reason: Number of subjects | Adverse event, serious fatal: 1 |
|----------------------------|---------------------------------|

| | |
|----------------------------|---------------------------------|
| Reason: Number of subjects | Consent withdrawn by subject: 1 |
|----------------------------|---------------------------------|

| | |
|----------------------------|--------------------------------|
| Reason: Number of subjects | not eligible for enrolment: 35 |
|----------------------------|--------------------------------|

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 119 patients were screened but only 82 patients were randomized to active treatment or placebo.

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

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|-----------|---------------|
| Arm title | placebo group |
|-----------|---------------|

Arm description:

saline and serum injected intramyocardially during CABG surgery

| | |
|----------|---------|
| Arm type | Placebo |
|----------|---------|

| | |
|----------------------------------------|---------|
| Investigational medicinal product name | placebo |
|----------------------------------------|---------|

| | |
|----------------------------------------|--|
| Investigational medicinal product code | |
|----------------------------------------|--|

| | |
|------------|--|
| Other name | |
|------------|--|

| | |
|----------------------|------------------------------------------------|
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
|----------------------|------------------------------------------------|

| | |
|--------------------------|------------------|
| Routes of administration | Intracardiac use |
|--------------------------|------------------|

Dosage and administration details:

The placebo consisted in 5 mL of physiological saline and 10% of autologous serum. The placebo was injected intramyocardially (divided in 15 injections or more) during coronary artery bypass graft (CABG) surgery.

| | |
|-----------|------------------------|
| Arm title | CD133+ treatment group |
|-----------|------------------------|

Arm description:

CD133+ cells injected intramyocardially during CABG surgery

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|----------------------------------------|------------------------------------------------|
| Investigational medicinal product name | CD133+ autologous bone marrow stem cells |
| Investigational medicinal product code | |
| Other name | CD133+ enriched bone marrow stem cells |
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
| Routes of administration | Intracardiac use |

Dosage and administration details:

The CD133+ cell preparation consisted in 5 mL of CD133+ cells (500,000-5,000,000 cells) suspended in physiological saline and 10% of autologous serum. The product (CD133+ cells) was injected intramyocardially (divided in 15 injections or more) during coronary artery bypass graft (CABG) surgery.

| Number of subjects in period 1 | placebo group | CD133+ treatment group |
|---------------------------------------------|---------------|------------------------|
| Started | 40 | 42 |
| Completed | 36 | 32 |
| Not completed | 4 | 10 |
| Consent withdrawn by subject | - | 2 |
| Adverse event, non-fatal | - | 5 |
| Body size does not allow MRI anymore | 1 | - |
| Pacemaker implantation | 1 | - |
| Cell preparation not eligible for treatment | - | 3 |
| Protocol deviation | 2 | - |

Baseline characteristics

Reporting groups

| | |
|-------------------------------------------------------------------------------------------------|------------------------|
| Reporting group title | placebo group |
| Reporting group description: saline and serum injected intramyocardially during CABG surgery | |
| Reporting group title | CD133+ treatment group |
| Reporting group description: CD133+ cells injected intramyocardially during CABG surgery | |

| Reporting group values | placebo group | CD133+ treatment group | Total |
|----------------------------------------------------|---------------|------------------------|-------|
| Number of subjects | 40 | 42 | 82 |
| Age categorical | | | |
| 18 years ≤ Age < 80 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) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Adults/Seniors (18-85 years) | 0 | 0 | 0 |
| 18 years ≤ Age < 80 years | 40 | 42 | 82 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 62.9 | 63 | |
| standard deviation | ± 8.49 | ± 8.72 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 6 | 5 | 11 |
| Male | 34 | 37 | 71 |

Subject analysis sets

| | |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|
| Subject analysis set title | Full Analysis Set (FAS/ITT) |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: A full analysis set (FAS) following the principle of intent-to-treat (ITT) had to include every patient randomized and compare the patients per group to which they were randomly allocated, regardless of patients' compliance, or withdrawal from the study. Confirmatory analyses on primary efficacy end-point was to be performed on the FAS patients. This ITT analysis was to be considered as the primary one. | |
| Subject analysis set title | Safety Analysis Set (SAS) |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: The safety population had to comprise all patients randomized into the study and treated. Safety | |

evaluations were to be performed on the safety population (SAS). All comparisons were to be executed per the group, to which the patients were randomized.

| | |
|----------------------------|------------------------|
| Subject analysis set title | Per Protocol Set (PPS) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

The per protocol set (PPS) was defined as a subset of the FAS/ITT patients who were compliant with the study protocol. The PPS sample had to consist of all patients from the FAS/ITT group without any major protocol violation. A secondary efficacy analysis of the primary endpoint had to be performed based upon the PPS, to assess the sensitivity of the analysis to the choice of analysis population.

| | |
|----------------------------|--------------------------------|
| Subject analysis set title | Safety Analysis Set II (SASII) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

In case treatment application violations were regarded as major violations during the blinded review meeting, and it was decided to analyse safety issues separately, two additional safety analysis sets SASII and SASIII which were not foreseen in the protocol were to be created. SASII had to consist of all patients who were treated correctly with 15 injections.

| | |
|----------------------------|----------------------------------|
| Subject analysis set title | Safety Analysis Set III (SASIII) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

In case treatment application violations were regarded as major violations during the blinded review meeting, and it was decided to analyse safety issues separately, two additional safety analysis sets SASII and SASIII which were not foreseen in the protocol were to be created. SASIII had to consist of all patients who were treated with more than 15 injections.

| | |
|----------------------------|-------------------------------------------------|
| Subject analysis set title | Insufficient CD 133+ Analysis Set (I-cd133+-AS) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Patients who received the cellular product or Placebo but were excluded from per protocol analysis set post-hoc because of cell count insufficiency were to be evaluated separately. This "Insufficient CD133+ Analysis Set"-Population (silent drop-outs) had to include every patient with a randomization number and a CD133+ cell count from $0.5 \times 10^6 > \text{CD133+ cell count} \geq 0.1 \times 10^6$. All comparisons in the I-CD133+- AS Population were to be executed per the group, to which the patients were randomized.

| Reporting group values | Full Analysis Set (FAS/ITT) | Safety Analysis Set (SAS) | Per Protocol Set (PPS) |
|----------------------------------------------------|-----------------------------|---------------------------|------------------------|
| Number of subjects | 82 | 77 | 58 |
| Age categorical | | | |
| 18 years ≤ Age < 80 years | | | |
| Units: Subjects | | | |
| In utero | | | |
| Preterm newborn infants (gestational age < 37 wks) | | | |
| Newborns (0-27 days) | | | |
| Infants and toddlers (28 days-23 months) | | | |
| Children (2-11 years) | | | |
| Adolescents (12-17 years) | | | |
| Adults (18-64 years) | | | |
| From 65-84 years | | | |
| 85 years and over | | | |
| Adults/Seniors (18-85 years) | | | |
| 18 years ≤ Age < 80 years | 82 | 77 | 58 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | ± | ± | ± |

| | | | |
|--------------------|--|--|--|
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | | | |
| Male | | | |

| Reporting group values | Safety Analysis Set II (SASII) | Safety Analysis Set III (SASIII) | Insufficient CD 133+ Analysis Set (I-cd133+-AS) |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------|----------------------------------|-------------------------------------------------|
| Number of subjects | 42 | 35 | 3 |
| Age categorical | | | |
| 18 years ≤ Age < 80 years | | | |
| Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over Adults/Seniors (18-85 years) 18 years ≤ Age < 80 years | 42 | 35 | 3 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | ± | ± | ± |
| standard deviation | | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | | | |
| Male | | | |

End points

End points reporting groups

| | |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------|
| Reporting group title | placebo group |
| Reporting group description: saline and serum injected intramyocardially during CABG surgery | |
| Reporting group title | CD133+ treatment group |
| Reporting group description: CD133+ cells injected intramyocardially during CABG surgery | |
| Subject analysis set title | Full Analysis Set (FAS/ITT) |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: A full analysis set (FAS) following the principle of intent-to-treat (ITT) had to include every patient randomized and compare the patients per group to which they were randomly allocated, regardless of patients' compliance, or withdrawal from the study. Confirmatory analyses on primary efficacy end-point was to be performed on the FAS patients. This ITT analysis was to be considered as the primary one. | |
| Subject analysis set title | Safety Analysis Set (SAS) |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: The safety population had to comprise all patients randomized into the study and treated. Safety evaluations were to be performed on the safety population (SAS). All comparisons were to be executed per the group, to which the patients were randomized. | |
| Subject analysis set title | Per Protocol Set (PPS) |
| Subject analysis set type | Per protocol |
| Subject analysis set description: The per protocol set (PPS) was defined as a subset of the FAS/ITT patients who were compliant with the study protocol. The PPS sample had to consist of all patients from the FAS/ITT group without any major protocol violation. A secondary efficacy analysis of the primary endpoint had to be performed based upon the PPS, to assess the sensitivity of the analysis to the choice of analysis population. | |
| Subject analysis set title | Safety Analysis Set II (SASII) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: In case treatment application violations were regarded as major violations during the blinded review meeting, and it was decided to analyse safety issues separately, two additional safety analysis sets SASII and SASIII which were not foreseen in the protocol were to be created. SASII had to consist of all patients who were treated correctly with 15 injections. | |
| Subject analysis set title | Safety Analysis Set III (SASIII) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: In case treatment application violations were regarded as major violations during the blinded review meeting, and it was decided to analyse safety issues separately, two additional safety analysis sets SASII and SASIII which were not foreseen in the protocol were to be created. SASIII had to consist of all patients who were treated with more than 15 injections. | |
| Subject analysis set title | Insufficient CD 133+ Analysis Set (I-cd133+-AS) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Patients who received the cellular product or Placebo but were excluded from per protocol analysis set post-hoc because of cell count insufficiency were to be evaluated separately. This "Insufficient CD133+ Analysis Set"-Population (silent drop-outs) had to include every patient with a randomization number and a CD133+ cell count from $0.5 \times 10^6 > \text{CD133+ cell count} \geq 0.1 \times 10^6$. All comparisons in the I-CD133+- AS Population were to be executed per the group, to which the patients were randomized. | |

Primary: LVEF at 6 months post-OP, measured by MRI at rest

| | |
|-----------------|---------------------------------------------------|
| End point title | LVEF at 6 months post-OP, measured by MRI at rest |
|-----------------|---------------------------------------------------|

End point description:

LVEF (left ventricular ejection fraction) at 6 months postoperatively, measured by MRI (magnetic resonance imaging) at rest and change in LVEF at 6 months post-OP compared with preoperatively (screening) and early postoperatively (discharge) as assessed by MRI. Cardiac MRI was established as the gold standard for determination of LV function (LVEF and LV volumes).

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

End point timeframe:

6 months postoperatively

| End point values | placebo group | CD133+ treatment group | | |
|----------------------------------|-------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 34 ^[1] | 30 ^[2] | | |
| Units: Percentage of LVEF | | | | |
| arithmetic mean (standard error) | 42.5 (± 9.65) | 44.1 (± 13.78) | | |

Notes:

[1] - arithmetic mean calculated out of 34 subjects

[2] - arithmetic mean calculated out of 30 subjects

Statistical analyses

| | |
|----------------------------|------------------|
| Statistical analysis title | Primary Analysis |
|----------------------------|------------------|

Statistical analysis description:

exploratory analysis of covariance (ANCOVA) adjusting for the covariates treatment, study sites and baseline LVEF.

| | |
|-------------------|----------------------------------------|
| Comparison groups | placebo group v CD133+ treatment group |
|-------------------|----------------------------------------|

| | |
|-----------------------------------------|----|
| Number of subjects included in analysis | 64 |
|-----------------------------------------|----|

| | |
|------------------------|---------------|
| Analysis specification | Pre-specified |
|------------------------|---------------|

| | |
|---------------|-------------|
| Analysis type | superiority |
|---------------|-------------|

| | |
|---------|-------------------------|
| P-value | = 0.8581 ^[3] |
|---------|-------------------------|

| | |
|--------|--------|
| Method | ANCOVA |
|--------|--------|

Notes:

[3] - =0.2855 (center)

=0.0205 (LVEF at baseline)

=0.7366 (Treatment*Center)

=0.8182 (treatment*LVEF at baseline)

=0.2760 (Center*LVEF at baseline)

=0.6660 (Treatment*Center*LVEF at baseline)

| | |
|----------------------------|---------------------|
| Statistical analysis title | Additional Analysis |
|----------------------------|---------------------|

Statistical analysis description:

mixed model analysis for repeat measures approach (MMRM) in order to compensate possible artefacts due to incomplete data groups

| | |
|-------------------|----------------------------------------|
| Comparison groups | placebo group v CD133+ treatment group |
|-------------------|----------------------------------------|

| | |
|-----------------------------------------|-----------------------|
| Number of subjects included in analysis | 64 |
| Analysis specification | Post-hoc |
| Analysis type | superiority |
| P-value | = 0.4454 |
| Method | Mixed models analysis |

Secondary: Change in LVEF at 6 month post-OP compared with preoperatively (screening) assessed by cardiac MRI scans

| | |
|-----------------|----------------------------------------------------------------------------------------------------------|
| End point title | Change in LVEF at 6 month post-OP compared with preoperatively (screening) assessed by cardiac MRI scans |
|-----------------|----------------------------------------------------------------------------------------------------------|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to 6 months post OP

| End point values | placebo group | CD133+ treatment group | | |
|----------------------------------|-----------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 34 | 30 | | |
| Units: Percentage of LVEF | | | | |
| arithmetic mean (standard error) | 8.0 (± 8.71) | 11.4 (± 13.52) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in LVEF at 6 month post-OP compared with preoperatively (screening) assessed by echocardiography

| | |
|-----------------|---------------------------------------------------------------------------------------------------------|
| End point title | Change in LVEF at 6 month post-OP compared with preoperatively (screening) assessed by echocardiography |
|-----------------|---------------------------------------------------------------------------------------------------------|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and 6 months post OP

| End point values | placebo group | CD133+ treatment group | | |
|----------------------------------|--------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 32 | 31 | | |
| Units: Percentage of LVEF | | | | |
| arithmetic mean (standard error) | 5.1 (\pm 10.73) | 6.0 (\pm 7.48) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in LVEF at 6 month post-OP compared with early postoperatively (discharge) assessed by cardiac MRI scans

| | |
|-----------------|-----------------------------------------------------------------------------------------------------------------|
| End point title | Change in LVEF at 6 month post-OP compared with early postoperatively (discharge) assessed by cardiac MRI scans |
|-----------------|-----------------------------------------------------------------------------------------------------------------|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and 6 months post OP

| End point values | placebo group | CD133+ treatment group | | |
|----------------------------------|-------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 14 | | |
| Units: Percentage of LVEF | | | | |
| arithmetic mean (standard error) | 4.1 (\pm 8.57) | 8.8 (\pm 6.38) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in LVEF at 6 month post-OP compared with early postoperatively (discharge) assessed by echocardiography

| | |
|-----------------|----------------------------------------------------------------------------------------------------------------|
| End point title | Change in LVEF at 6 month post-OP compared with early postoperatively (discharge) assessed by echocardiography |
|-----------------|----------------------------------------------------------------------------------------------------------------|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and 6 months post OP

| End point values | placebo group | CD133+ treatment group | | |
|----------------------------------|-----------------|------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 28 | 30 | | |
| Units: Percentage of LVEF | | | | |
| arithmetic mean (standard error) | 4.5 (± 9.70) | 4.3 (± 5.82) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events collected between start of screening and end of main trial phase

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 15.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------|
| Reporting group title | CD133+ |
|-----------------------|--------|

Reporting group description: -

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

Reporting group description: -

| Serious adverse events | CD133+ | Placebo | |
|------------------------------------------------------|------------------|------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 19 / 37 (51.35%) | 15 / 40 (37.50%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Vascular disorders | | | |
| Thrombosis | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 40 (2.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Surgical and medical procedures | | | |
| Implantable defibrillator insertion | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 40 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Impaired healing | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 40 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |

| | | | |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 40 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Epididymitis | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 40 (2.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 40 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 40 (2.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumothorax | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 40 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| In-stent coronary artery restenosis | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 40 (2.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Postoperative thoracic procedure complication | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 40 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |

| | | | |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 40 (2.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 3 / 37 (8.11%) | 1 / 40 (2.50%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial flutter | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 40 (2.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bradycardia | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 40 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 40 (2.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 1 / 40 (2.50%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiovascular insufficiency | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 40 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intracardiac thrombus | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 40 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pericardial effusion | | | |

| | | | |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed | 1 / 37 (2.70%) | 1 / 40 (2.50%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tachycardia | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 40 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular fibrillation | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 40 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 2 / 40 (5.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 40 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 40 (2.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Visual impairment | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 40 (2.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |

| | | | |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 40 (2.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Skin haemorrhage | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 40 (2.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Renal failure | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 1 / 40 (2.50%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Diabetic foot infection | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 2 / 40 (5.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes zoster | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 40 (2.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung infection | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 1 / 40 (2.50%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 2 / 40 (5.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Postoperative wound infection | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 40 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|-------------------------------------------------|----------------|----------------|--|
| Sepsis | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 40 (2.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound infection | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 40 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | CD133+ | Placebo | |
|-------------------------------------------------------|------------------|-------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 36 / 37 (97.30%) | 40 / 40 (100.00%) | |
| Vascular disorders | | | |
| Haematoma | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 2 / 40 (5.00%) | |
| occurrences (all) | 2 | 2 | |
| Hypertension | | | |
| subjects affected / exposed | 3 / 37 (8.11%) | 4 / 40 (10.00%) | |
| occurrences (all) | 3 | 5 | |
| Hypertensive crisis | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 2 / 40 (5.00%) | |
| occurrences (all) | 0 | 2 | |
| Thrombophlebitis | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 2 / 40 (5.00%) | |
| occurrences (all) | 0 | 2 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 3 / 40 (7.50%) | |
| occurrences (all) | 1 | 3 | |
| Chest pain | | | |
| subjects affected / exposed | 4 / 37 (10.81%) | 2 / 40 (5.00%) | |
| occurrences (all) | 5 | 2 | |
| Impaired healing | | | |

| | | | |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed | 4 / 37 (10.81%) | 3 / 40 (7.50%) | |
| occurrences (all) | 4 | 3 | |
| Oedema | | | |
| subjects affected / exposed | 8 / 37 (21.62%) | 12 / 40 (30.00%) | |
| occurrences (all) | 10 | 15 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 10 / 37 (27.03%) | 14 / 40 (35.00%) | |
| occurrences (all) | 12 | 16 | |
| Pain | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 1 / 40 (2.50%) | |
| occurrences (all) | 2 | 1 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Atelectasis | | | |
| subjects affected / exposed | 3 / 37 (8.11%) | 2 / 40 (5.00%) | |
| occurrences (all) | 3 | 2 | |
| Cough | | | |
| subjects affected / exposed | 9 / 37 (24.32%) | 7 / 40 (17.50%) | |
| occurrences (all) | 10 | 7 | |
| Dyspnoea | | | |
| subjects affected / exposed | 3 / 37 (8.11%) | 3 / 40 (7.50%) | |
| occurrences (all) | 3 | 3 | |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 3 / 37 (8.11%) | 3 / 40 (7.50%) | |
| occurrences (all) | 3 | 3 | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 2 / 40 (5.00%) | |
| occurrences (all) | 0 | 2 | |
| Pleural effusion | | | |
| subjects affected / exposed | 19 / 37 (51.35%) | 20 / 40 (50.00%) | |
| occurrences (all) | 20 | 21 | |
| Pneumothorax | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 1 / 40 (2.50%) | |
| occurrences (all) | 3 | 1 | |
| Psychiatric disorders | | | |

| | | | |
|---------------------------------------------------------------------------------------------------------------|----------------------|----------------------|--|
| Insomnia subjects affected / exposed occurrences (all) | 5 / 37 (13.51%) 6 | 5 / 40 (12.50%) 5 | |
| Sleep disorder subjects affected / exposed occurrences (all) | 4 / 37 (10.81%) 4 | 5 / 40 (12.50%) 5 | |
| Investigations | | | |
| Blood creatine phosphokinase increased subjects affected / exposed occurrences (all) | 1 / 37 (2.70%) 1 | 2 / 40 (5.00%) 4 | |
| C-reactive protein increased subjects affected / exposed occurrences (all) | 5 / 37 (13.51%) 5 | 3 / 40 (7.50%) 4 | |
| Electrocardiogram QT prolonged subjects affected / exposed occurrences (all) | 1 / 37 (2.70%) 1 | 3 / 40 (7.50%) 3 | |
| Haemoglobin decreased subjects affected / exposed occurrences (all) | 1 / 37 (2.70%) 2 | 2 / 40 (5.00%) 2 | |
| N-terminal prohormone brain natriuretic peptide increased subjects affected / exposed occurrences (all) | 3 / 37 (8.11%) 3 | 1 / 40 (2.50%) 2 | |
| Troponin T increased subjects affected / exposed occurrences (all) | 2 / 37 (5.41%) 2 | 0 / 40 (0.00%) 0 | |
| Urine output decreased subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 2 / 40 (5.00%) 2 | |
| Injury, poisoning and procedural complications | | | |
| Injury subjects affected / exposed occurrences (all) | 8 / 37 (21.62%) 9 | 9 / 40 (22.50%) 9 | |
| Procedural pain subjects affected / exposed occurrences (all) | 2 / 37 (5.41%) 2 | 1 / 40 (2.50%) 1 | |

| | | | |
|-----------------------------------------------------------------------------------------|----------------------|----------------------|--|
| Wound secretion subjects affected / exposed occurrences (all) | 1 / 37 (2.70%) 1 | 2 / 40 (5.00%) 2 | |
| Cardiac disorders | | | |
| Angina pectoris subjects affected / exposed occurrences (all) | 2 / 37 (5.41%) 3 | 0 / 40 (0.00%) 0 | |
| Arrhythmia subjects affected / exposed occurrences (all) | 2 / 37 (5.41%) 2 | 0 / 40 (0.00%) 0 | |
| Arrhythmia supraventricular subjects affected / exposed occurrences (all) | 1 / 37 (2.70%) 1 | 2 / 40 (5.00%) 2 | |
| Atrial fibrillation subjects affected / exposed occurrences (all) | 7 / 37 (18.92%) 9 | 9 / 40 (22.50%) 9 | |
| Atrioventricular block subjects affected / exposed occurrences (all) | 2 / 37 (5.41%) 2 | 0 / 40 (0.00%) 0 | |
| Atrioventricular block first degree subjects affected / exposed occurrences (all) | 2 / 37 (5.41%) 2 | 1 / 40 (2.50%) 1 | |
| Bradycardia subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 5 / 40 (12.50%) 6 | |
| Bundle branch block left subjects affected / exposed occurrences (all) | 3 / 37 (8.11%) 3 | 1 / 40 (2.50%) 1 | |
| Pericardial effusion subjects affected / exposed occurrences (all) | 6 / 37 (16.22%) 6 | 7 / 40 (17.50%) 7 | |
| Supraventricular extrasystoles subjects affected / exposed occurrences (all) | 1 / 37 (2.70%) 1 | 2 / 40 (5.00%) 2 | |
| Supraventricular tachyarrhythmia | | | |

| | | | |
|--------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 3 / 37 (8.11%) | 2 / 40 (5.00%) | |
| occurrences (all) | 5 | 3 | |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 3 / 37 (8.11%) | 0 / 40 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 2 / 40 (5.00%) | |
| occurrences (all) | 0 | 2 | |
| Ventricular arrhythmia | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 2 / 40 (5.00%) | |
| occurrences (all) | 2 | 2 | |
| Ventricular extrasystoles | | | |
| subjects affected / exposed | 4 / 37 (10.81%) | 2 / 40 (5.00%) | |
| occurrences (all) | 4 | 2 | |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 2 / 40 (5.00%) | |
| occurrences (all) | 0 | 2 | |
| Nervous system disorders | | | |
| Syncope | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 2 / 40 (5.00%) | |
| occurrences (all) | 1 | 2 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 7 / 37 (18.92%) | 6 / 40 (15.00%) | |
| occurrences (all) | 8 | 6 | |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 2 / 40 (5.00%) | |
| occurrences (all) | 0 | 2 | |
| Gastrointestinal disorders | | | |
| Constipation | | | |
| subjects affected / exposed | 6 / 37 (16.22%) | 7 / 40 (17.50%) | |
| occurrences (all) | 6 | 7 | |
| Nausea | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 3 / 40 (7.50%) | |
| occurrences (all) | 2 | 3 | |
| Vomiting | | | |

| | | | |
|--------------------------------------------------|---------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 3 / 40 (7.50%) 3 | |
| Skin and subcutaneous tissue disorders | | | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 0 / 40 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Scar pain | | | |
| subjects affected / exposed | 3 / 37 (8.11%) | 1 / 40 (2.50%) | |
| occurrences (all) | 3 | 2 | |
| Renal and urinary disorders | | | |
| Nocturia | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 2 / 40 (5.00%) | |
| occurrences (all) | 0 | 2 | |
| Renal failure | | | |
| subjects affected / exposed | 3 / 37 (8.11%) | 1 / 40 (2.50%) | |
| occurrences (all) | 4 | 1 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 6 / 40 (15.00%) | |
| occurrences (all) | 1 | 6 | |
| Joint effusion | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 5 / 40 (12.50%) | |
| occurrences (all) | 2 | 5 | |
| Muscle tightness | | | |
| subjects affected / exposed | 3 / 37 (8.11%) | 3 / 40 (7.50%) | |
| occurrences (all) | 4 | 3 | |
| Neck pain | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 1 / 40 (2.50%) | |
| occurrences (all) | 2 | 1 | |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 2 / 40 (5.00%) | |
| occurrences (all) | 0 | 2 | |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 3 / 40 (7.50%) | |
| occurrences (all) | 1 | 3 | |
| Infections and infestations | | | |

| | | | |
|------------------------------------------------------------------------------|----------------------|---------------------|--|
| Device related infection subjects affected / exposed occurrences (all) | 2 / 37 (5.41%) 2 | 0 / 40 (0.00%) 0 | |
| Lung infection subjects affected / exposed occurrences (all) | 1 / 37 (2.70%) 1 | 2 / 40 (5.00%) 2 | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 1 / 37 (2.70%) 1 | 2 / 40 (5.00%) 2 | |
| Pneumonia subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 2 / 40 (5.00%) 2 | |
| Metabolism and nutrition disorders | | | |
| Fluid retention subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 2 / 40 (5.00%) 2 | |
| Hyperglycaemia subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 2 / 40 (5.00%) 2 | |
| Hypokalaemia subjects affected / exposed occurrences (all) | 5 / 37 (13.51%) 6 | 3 / 40 (7.50%) 4 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 02 July 2009 | Change of Sponsorship; change of Stem Cell Manufacturer/Central Laboratory Cell Processing; IMP: range of the amount of cells applied was expanded from 5-10x10 ⁶ CD133+ cells to 1-10x10 ⁶ CD133+ in order to be in accordance with the range applied in the preceding phase I/II trials; moderate revision to Inclusion and exclusion criteria, Revision of AE Section: Start of documentation changed from Assessment IIa to the date of IC (Assessment I); IC: Text regarding time given to patients for considerations changed |
| 18 December 2009 | Medical Director at sponsor changed; LVEF for inclusion changed from $\leq 35\%$ to $25\% \leq \text{LVEF} \leq 40\%$ |
| 20 December 2010 | Restart of recruitment; Threshold for cell number changed to 0.5 Mio -5 Mio; EQ-5D questionnaire implemented |
| 09 June 2011 | New sites; Change of Coordinating Investigator |
| 18 November 2011 | LVEF threshold risen to $\leq 50\%$; prolongation of recruitment time from 2 to 3 years, total study duration increased to 3.5 years |
| 17 August 2012 | Interim analysis after 70 patients completed 6-Months follow up; study duration extended by 1 year |
| 27 April 2016 | Recruitment Stop 12 Nov 2015 due to decrease in availability of eligible patients; sponsor study responsible physician changed; Core lab responsibility changed |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|-------------------|----------------------------------------------------------------------------------------------------------------------------------|------------------|
| 08 September 2010 | Voluntary hold of recruitment: Cell number of at least 1 Mio CD 133+ cells not reached in two patients. Root cause analysis done | 20 December 2010 |

Notes:

Limitations and caveats

None reported