



## Clinical trial results:

**Regeneration of ischemic damages in cardiovascular system using Wharton's jelly as an unlimited source of mesenchymal stem cells for regenerative medicine.**

**Project of the National Centre for Research and Development (Poland) 'STRATEGMED II'.**

**Cardiovascular Clinical Project to Evaluate the Regenerative Capacity of CardioCell in patients with acute myocardial infarction (AMI).**

### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2016-004662-25   |
| Trial protocol           | PL               |
| Global end of trial date | 16 February 2021 |

### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 14 October 2022 |
| First version publication date | 14 October 2022 |

### Trial information

#### Trial identification

|                       |           |
|-----------------------|-----------|
| Sponsor protocol code | AMI-Study |
|-----------------------|-----------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03404063 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Krakowski Szpital Specjalistyczny im. Jana Pawła II   |
| Sponsor organisation address | Pradnicka 80, Krakow, Poland, 31-202  |
| Public contact               | Clinical Trial Information Desk, Ewa Gąsior, 48 126142000, e.gasior@szpitaljp2.krakow.pl            |
| Scientific contact           | Principal Investigator, Piotr Musiałek MD, PhD, 48 126142000, badaniakliniczne@szpitaljp2.krakow.pl |

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                       | 25 August 2021   |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 16 February 2021 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

Regeneration of ischemic damages in cardiovascular system using Wharton's jelly as an unlimited source of mesenchymal stem cells for regenerative medicine.

Project of the National Centre for Research and Development (Poland) 'STRATEGMED II'.

Cardiovascular Clinical Project to Evaluate the Regenerative Capacity of CardioCell in patients with acute myocardial infarction (AMI).

Protection of trial subjects:

The Principal Investigator (PI) retains overall responsibility for the informed consent of participants at their site and must ensure that any person delegated responsibility to participate in the informed consent process is duly authorized, trained and competent to participate according to the ethically approved protocol, principles of Good Clinical Practice (GCP) and Declaration of Helsinki.

In order to constitute evidence with respect to product safety, regulatory and legal compliance, the investigator agrees to retain project related documents in a location which is secure and to which access can be gained if required. The following documents must be archived: the investigators file with respect to all required GCP documents, including signed patient informed consent forms, CRFs and monitoring forms. Data reported into eCRF will be anonymized by patients code. The list with assigned code numbers will be stored in Investigation Centre and will not be shared.

The Sponsor has ethical, legal and scientific obligations to carefully follow this project in a detailed and orderly manner in accordance with established research principles and applicable regulations. The investigator, as part of his responsibilities, is expected to cooperate with the Sponsor in ensuring that the project adheres to the protocol and GCP requirements. As part of a concerted effort to fulfil these obligations, the Sponsor will authorize a Clinical research Organization (CRO) to perform monitoring tasks and visit the centers during the project. The processes reviewed can relate to participant enrolment, consent, eligibility, and allocation to trial groups; adherence to trial interventions and policies to protect participants, including reporting of harm and completeness, accuracy, and timeliness of data collection. The investigator will permit the Sponsor' authorized CRO personnel to monitor the project as frequently as is deemed necessary and provide access to medical records.

Background therapy: -

Evidence for comparator: -

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 20 October 2017 |
| Long term follow-up planned                               | No              |
| Independent data monitoring committee (IDMC) involvement? | No              |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |             |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Poland: 115 |
| Worldwide total number of subjects   | 115         |
| EEA total number of subjects         | 115         |

Notes:

| <b>Subjects enrolled per age group</b>    |    |
|---|----|
| 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)                      | 78 |
| From 65 to 84 years                       | 37 |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

All patients who provided informed consent and met inclusion criteria without any exclusion criteria were enrolled to the study.

### 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 |

### Arms

|                              |              |
|------------------------------|--------------|
| Are arms mutually exclusive? | Yes          |
| <b>Arm title</b>             | active group |

Arm description: -

|  |                          |
|--|--------------------------|
| Arm type                               | Experimental             |
| Investigational medicinal product name | CardioCell               |
| Investigational medicinal product code |                          |
| Other name                             |                          |
| Pharmaceutical forms                   | Suspension for injection |
| Routes of administration               | Intracoronary use        |

Dosage and administration details:

Patients randomized to the active treatment group: Transcoronary or trans-bypass graft administration of 30 000 000 cells (suspended in 20 ml of 0.9% NaCl and 5% albumin) was performed using a dedicated cell delivery catheter.

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

Arm description: -

|  |                        |
|--|------------------------|
| Arm type                               | Placebo                |
| Investigational medicinal product name | Cardio-cell placebo    |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intracoronary use      |

Dosage and administration details:

Patients randomized to the placebo group: 0.9% NaCl and 5% albumin injections (in the same volumes as CardioCell) via the coronary arter(ies)/bypass grafts. The CardioCell and placebo are distributed encoded, in an indistinguishable form.

| Number of subjects in period<br>1 <sup>[1]</sup> | active group | placebo |
|--|--------------|---------|
|  |              |         |
| Started  | 70           | 35      |
| Completed  | 67           | 33      |
| Not completed                                    | 3            | 2       |
| Adverse event, serious fatal                     | 2            | 2       |
| Lost to follow-up                                | 1            | -       |

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Notes:

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

Justification: 10 patients were enrolled as a pilot cohort according to protocol

## Baseline characteristics

## End points

### End points reporting groups

|                                |              |
|--------------------------------|--------------|
| Reporting group title          | active group |
| Reporting group description: - |              |
| Reporting group title          | placebo      |
| Reporting group description: - |              |

### Primary: IS of the LV muscle (cMRI) change1

|  |                                    |
|--|------------------------------------|
| End point title  | IS of the LV muscle (cMRI) change1 |
| End point description:<br>IS (infarct size) of the LV (left ventricle) muscle (cMRI) change between baseline and 6 months FU |                                    |
| End point type   | Primary                            |
| End point timeframe:<br>baseline vs 6 months FU  |                                    |

| End point values                      | active group            | placebo                 |  |  |
|---------------------------------------|-------------------------|-------------------------|--|--|
| Subject group type                    | Reporting group         | Reporting group         |  |  |
| Number of subjects analysed           | 58                      | 29                      |  |  |
| Units: percent                        |                         |                         |  |  |
| median (inter-quartile range (Q1-Q3)) | -6.36 (-11.46 to -2.41) | -9.54 (-19.93 to -4.74) |  |  |

### Statistical analyses

|   |                                   |
|---|-----------------------------------|
| Statistical analysis title              | IS of the LV muscle (cMRI) change |
| Comparison groups                       | placebo v active group            |
| Number of subjects included in analysis | 87                                |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           | superiority                       |
| P-value                                 | = 0.0171                          |
| Method                                  | t-test, 2-sided                   |

### Secondary: IS of the LV muscle (SPECT) change

|  |                                    |
|--|------------------------------------|
| End point title  | IS of the LV muscle (SPECT) change |
| End point description:<br>IS of the LV muscle (SPECT) change |                                    |
| End point type   | Secondary                          |
| End point timeframe:<br>baseline vs 6 months FU              |                                    |

| <b>End point values</b>               | active group       | placebo              |  |  |
|---------------------------------------|--------------------|----------------------|--|--|
| Subject group type                    | Reporting group    | Reporting group      |  |  |
| Number of subjects analysed           | 68                 | 33                   |  |  |
| Units: number                         |                    |                      |  |  |
| median (inter-quartile range (Q1-Q3)) | -1.0 (-6.0 to 2.0) | -1.0 (-9.50 to 3.00) |  |  |

### Statistical analyses

|   |                                    |
|---|------------------------------------|
| <b>Statistical analysis title</b>       | IS of the LV muscle (SPECT) change |
| Comparison groups                       | active group v placebo             |
| Number of subjects included in analysis | 101                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           | superiority                        |
| P-value                                 | = 0.6478                           |
| Method                                  | Wilcoxon (Mann-Whitney)            |

### Secondary: LVEF (cMRI) change

|  |                    |
|--|--------------------|
| End point title  | LVEF (cMRI) change |
| End point description:<br>LVEF- left ventricle ejection fraction (cMRI- cardiac magnetic resonance ) change between baseline and 6 months FU |                    |
| End point type   | Secondary          |
| End point timeframe:<br>baseline vs 6 months FU  |                    |

| <b>End point values</b>               | active group          | placebo             |  |  |
|---------------------------------------|-----------------------|---------------------|--|--|
| Subject group type                    | Reporting group       | Reporting group     |  |  |
| Number of subjects analysed           | 63                    | 31                  |  |  |
| Units: number                         |                       |                     |  |  |
| median (inter-quartile range (Q1-Q3)) | 4.00 (-1.00 to 11.00) | 6.00 (3.00 to 9.00) |  |  |

### Statistical analyses

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | LVEF (cMRI) change     |
| Comparison groups                 | active group v placebo |



|   |                         |
|---|-------------------------|
| Number of subjects included in analysis | 94                      |
| Analysis specification                  | Pre-specified           |
| Analysis type                           | superiority             |
| P-value                                 | = 0.3319                |
| Method                                  | Wilcoxon (Mann-Whitney) |

### Secondary: LVEF (SPECT) change

|                        |   |
|------------------------|---|
| End point title        | LVEF (SPECT) change   |
| End point description: | LVEF (left ventricle ejection fraction) (SPECT) change between baseline and 6 months FU |
| End point type         | Secondary   |
| End point timeframe:   | baseline vs 6 months FU   |

| End point values                      | active group         | placebo              |  |  |
|---------------------------------------|----------------------|----------------------|--|--|
| Subject group type                    | Reporting group      | Reporting group      |  |  |
| Number of subjects analysed           | 69                   | 33                   |  |  |
| Units: number                         |                      |                      |  |  |
| median (inter-quartile range (Q1-Q3)) | 3.00 (-2.00 to 7.00) | 3.00 (-0.50 to 7.00) |  |  |

### Statistical analyses

|   |                        |
|---|------------------------|
| Statistical analysis title              | LVEF (SPECT) change    |
| Comparison groups                       | active group v placebo |
| Number of subjects included in analysis | 102                    |
| Analysis specification                  | Pre-specified          |
| Analysis type                           | superiority            |
| P-value                                 | = 0.3965               |
| Method                                  | t-test, 2-sided        |

### Secondary: LVEF (echo) change

|                        |   |
|------------------------|---|
| End point title        | LVEF (echo) change  |
| End point description: | LVEF- left ventricle ejection fraction (echo) change between baseline and 6 months FU |
| End point type         | Secondary   |
| End point timeframe:   | baseline vs 6 months FU   |

| <b>End point values</b>               | active group        | placebo              |  |  |
|---------------------------------------|---------------------|----------------------|--|--|
| Subject group type                    | Reporting group     | Reporting group      |  |  |
| Number of subjects analysed           | 68                  | 33                   |  |  |
| Units: number                         |                     |                      |  |  |
| median (inter-quartile range (Q1-Q3)) | 3.50 (0.25 to 8.00) | 7.00 (1.50 to 10.00) |  |  |

### Statistical analyses

| <b>Statistical analysis title</b>       | LVEF (echo) change     |
|---|------------------------|
| Comparison groups                       | active group v placebo |
| Number of subjects included in analysis | 101                    |
| Analysis specification                  | Pre-specified          |
| Analysis type                           | superiority            |
| P-value                                 | = 0.2067               |
| Method                                  | t-test, 2-sided        |

### Secondary: Death, MI and/or hospitalization for HF - up to 365 days after procedure

| <b>End point title</b> | Death, MI and/or hospitalization for HF - up to 365 days after procedure                      |
|------------------------|---|
| End point description: | Death, MI (myocardial infarct) and/or hospitalization for HF - up to 365 days after procedure |
| End point type         | Secondary   |
| End point timeframe:   | baselien vs 6 months FU   |

| <b>End point values</b>     | active group    | placebo         |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 70              | 35              |  |  |
| Units: number               | 5               | 5               |  |  |

### Statistical analyses

| <b>Statistical analysis title</b> | Death, MI and/or hospitalization for HF during obs |
|-----------------------------------|--|
| Comparison groups                 | active group v placebo                             |

|   |               |
|---|---------------|
| Number of subjects included in analysis | 105           |
| Analysis specification                  | Pre-specified |
| Analysis type                           | superiority   |
| P-value                                 | = 0.2953      |
| Method                                  | Fisher exact  |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported in patients from personal consent and study enrollment to last visit in the study.

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

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 24.1   |

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | overall trial |
|-----------------------|---------------|

Reporting group description: -

| Serious adverse events                            | overall trial                                      |  |  |
|---|--|--|--|
| Total subjects affected by serious adverse events |  |  |  |
| subjects affected / exposed                       | 21 / 105 (20.00%)                                  |  |  |
| number of deaths (all causes)                     | 5  |  |  |
| number of deaths resulting from adverse events    | 5  |  |  |
| Investigations                                    |  |  |  |
| Cardiac stress test abnormal                      |  |  |  |
| subjects affected / exposed                       | 1 / 105 (0.95%)                                    |  |  |
| occurrences causally related to treatment / all   | 0 / 1  |  |  |
| deaths causally related to treatment / all        | 0 / 0  |  |  |
| Vascular disorders                                |  |  |  |
| Critical limb ischaemia                           |  |  |  |
| subjects affected / exposed                       | 1 / 105 (0.95%)                                    |  |  |
| occurrences causally related to treatment / all   | 0 / 1  |  |  |
| deaths causally related to treatment / all        | 0 / 1  |  |  |
| Cardiac disorders                                 |  |  |  |
| Cardiac failure                                   | Additional description: cardiac failure aggravated |  |  |
| subjects affected / exposed                       | 7 / 105 (6.67%)                                    |  |  |
| occurrences causally related to treatment / all   | 0 / 15   |  |  |
| deaths causally related to treatment / all        | 0 / 1  |  |  |
| Cardiac arrest                                    |  |  |  |
| subjects affected / exposed                       | 3 / 105 (2.86%)                                    |  |  |
| occurrences causally related to treatment / all   | 0 / 3  |  |  |
| deaths causally related to treatment / all        | 0 / 3  |  |  |

|   |   |  |  |
|---|---|--|--|
| Coronary artery disease progression<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                     | Additional description: Coronary artery disease progression |  |  |
|   | 2 / 105 (1.90%)   |  |  |
|   | 0 / 3   |  |  |
|   | 0 / 0   |  |  |
| ventricular arrhythmia<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                  | 2 / 105 (1.90%)   |  |  |
|   | 0 / 2   |  |  |
|   | 0 / 0   |  |  |
|   |   |  |  |
| unstable angina<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all   | 3 / 105 (2.86%)   |  |  |
|   | 0 / 3   |  |  |
|   | 0 / 0   |  |  |
|   |   |  |  |
| Nervous system disorders<br>Ischemic stroke<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all             | 1 / 105 (0.95%)   |  |  |
|   | 0 / 1   |  |  |
|   | 0 / 1   |  |  |
|   |   |  |  |
| Transient ischemic attack<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                               | 1 / 105 (0.95%)   |  |  |
|   | 0 / 1   |  |  |
|   | 0 / 0   |  |  |
|   |   |  |  |
| Gastrointestinal disorders<br>Gastrointestinal bleeding<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 2 / 105 (1.90%)   |  |  |
|   | 0 / 2   |  |  |
|   | 0 / 0   |  |  |
|   |   |  |  |
| Renal and urinary disorders<br>Acute prerenal failure<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all   | 1 / 105 (0.95%)   |  |  |
|   | 0 / 1   |  |  |
|   | 0 / 0   |  |  |
|   |   |  |  |
| Infections and infestations<br>Bacterial sepsis   |   |  |  |
|   |   |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 105 (0.95%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

Frequency threshold for reporting non-serious adverse events: 0 %

| <b>Non-serious adverse events</b>                     | overall trial  |  |  |
|---|--|--|--|
| Total subjects affected by non-serious adverse events |  |  |  |
| subjects affected / exposed                           | 58 / 105 (55.24%)  |  |  |
| Cardiac disorders                                     |  |  |  |
| ICD implantation                                      |  |  |  |
| subjects affected / exposed                           | 11 / 105 (10.48%)  |  |  |
| occurrences (all)                                     | 11   |  |  |
| planned PCI   | Additional description: planned PCI performed prior to study procedure |  |  |
| subjects affected / exposed                           | 17 / 105 (16.19%)  |  |  |
| occurrences (all)                                     | 17   |  |  |
| planned carotid artery stenting                       |  |  |  |
| subjects affected / exposed                           | 3 / 105 (2.86%)  |  |  |
| occurrences (all)                                     | 3  |  |  |
| left ventricle thrombus                               |  |  |  |
| subjects affected / exposed                           | 3 / 105 (2.86%)  |  |  |
| occurrences (all)                                     | 3  |  |  |
| mil arrhythmia  |  |  |  |
| subjects affected / exposed                           | 2 / 105 (1.90%)  |  |  |
| occurrences (all)                                     | 2  |  |  |
| chest pain  |  |  |  |
| subjects affected / exposed                           | 3 / 105 (2.86%)  |  |  |
| occurrences (all)                                     | 4  |  |  |
| control angiography                                   |  |  |  |
| subjects affected / exposed                           | 2 / 105 (1.90%)  |  |  |
| occurrences (all)                                     | 2  |  |  |
| heart failure optimisation                            |  |  |  |
| subjects affected / exposed                           | 4 / 105 (3.81%)  |  |  |
| occurrences (all)                                     | 4  |  |  |
| hypotonia and fainting                                |  |  |  |

|   |  |  |  |
|---|--|--|--|
| subjects affected / exposed                     | 2 / 105 (1.90%)                              |  |  |
| occurrences (all)                               | 2  |  |  |
| pericardial effusion                            |  |  |  |
| subjects affected / exposed                     | 2 / 105 (1.90%)                              |  |  |
| occurrences (all)                               | 2  |  |  |
| poor blood pressure control                     |  |  |  |
| subjects affected / exposed                     | 1 / 105 (0.95%)                              |  |  |
| occurrences (all)                               | 1  |  |  |
| Gastrointestinal disorders                      |  |  |  |
| cholelithiasis causing bilious colic            |  |  |  |
| subjects affected / exposed                     | 1 / 105 (0.95%)                              |  |  |
| occurrences (all)                               | 1  |  |  |
| diarrhoea                                       |  |  |  |
| subjects affected / exposed                     | 1 / 105 (0.95%)                              |  |  |
| occurrences (all)                               | 1  |  |  |
| Respiratory, thoracic and mediastinal disorders |  |  |  |
| pneumonia                                       |  |  |  |
| subjects affected / exposed                     | 3 / 105 (2.86%)                              |  |  |
| occurrences (all)                               | 3  |  |  |
| Skin and subcutaneous tissue disorders          |  |  |  |
| rash  | Additional description: rash after procedure |  |  |
| subjects affected / exposed                     | 3 / 105 (2.86%)                              |  |  |
| occurrences (all)                               | 3  |  |  |
| Epistaxis                                       |  |  |  |
| subjects affected / exposed                     | 2 / 105 (1.90%)                              |  |  |
| occurrences (all)                               | 2  |  |  |
| hematoma on thigh                               |  |  |  |
| subjects affected / exposed                     | 1 / 105 (0.95%)                              |  |  |
| occurrences (all)                               | 1  |  |  |
| Renal and urinary disorders                     |  |  |  |
| Urinary tract infection                         |  |  |  |
| subjects affected / exposed                     | 3 / 105 (2.86%)                              |  |  |
| occurrences (all)                               | 3  |  |  |
| vaginal bleeding                                |  |  |  |
| subjects affected / exposed                     | 1 / 105 (0.95%)                              |  |  |
| occurrences (all)                               | 1  |  |  |

|   |  |  |  |
|---|--|--|--|
| urinary retention<br>subjects affected / exposed<br>occurrences (all)   | 1 / 105 (0.95%)<br>1                                 |  |  |
| Nephropathy<br>subjects affected / exposed<br>occurrences (all)   | 1 / 105 (0.95%)<br>1                                 |  |  |
| Renal colic<br>subjects affected / exposed<br>occurrences (all)   | 1 / 105 (0.95%)<br>1                                 |  |  |
| Endocrine disorders<br>Diabetes mellitus inadequate control<br>subjects affected / exposed<br>occurrences (all) | 2 / 105 (1.90%)<br>2                                 |  |  |
| Musculoskeletal and connective tissue disorders   |  |  |  |
| Chills  | Additional description: chills after study procedure |  |  |
| subjects affected / exposed<br>occurrences (all)  | 7 / 105 (6.67%)<br>7                                 |  |  |
| Fracture of left fibula<br>subjects affected / exposed<br>occurrences (all)                                     | 1 / 105 (0.95%)<br>1                                 |  |  |
| Infections and infestations<br>mild/moderate infection<br>subjects affected / exposed<br>occurrences (all)      | 4 / 105 (3.81%)<br>4                                 |  |  |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment   |
|------------------|---|
| 14 July 2017     | Version 2.0 - following the decision to split CIRCULATE project into three separate clinical trials a version of the protocol was prepared in which the investigated medical condition was acute myocardial infarction (AMI). |
| 12 February 2019 | Version 3.0- data of new study sites was added, description of study catheter was clarified, information about additional blood collections was added.  |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported