



## Clinical trial results: Double-Blind, Randomized, Placebo-Controlled, Phase 2 Safety and Efficacy Trial of MultiStem® in Adults With Ischemic Stroke

### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2012-005749-18   |
| Trial protocol           | GB               |
| Global end of trial date | 07 December 2015 |

### Results information

|                                   |                                                                                                                                                                                    |
|-----------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Result version number             | v1 (current)                                                                                                                                                                       |
| This version publication date     | 14 May 2021                                                                                                                                                                        |
| First version publication date    | 14 May 2021                                                                                                                                                                        |
| Summary attachment (see zip file) | Hess 2017 (Hess (Mays) 2017 - Safety and efficacy of MAPC in ischaemic stroke MASTERS phase 2 trial.pdf)<br>Hess 2017 - Supplement (Hess (Mays) 2017 - Supplementary Appendix.pdf) |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | B01-02 |
|-----------------------|--------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01436487 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |                                                                 |
|------------------------------|-----------------------------------------------------------------|
| Sponsor organisation name    | ReGenesys, BVBA                                                 |
| Sponsor organisation address | Gaston Geenslaan 1, Heverlee, Belgium, 3001                     |
| Public contact               | Manal Morsy, ReGenesys, BVBA, 1 2162153071, mmorsy@regenesys.eu |
| Scientific contact           | Manal Morsy, ReGenesys, BVBA, 1 2162153071, mmorsy@regenesys.eu |

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                       | 07 December 2015 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 07 December 2015 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 07 December 2015 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

The primary objectives of this study are to:

-To determine the highest well tolerated and safest single dose of MultiStem up to a maximum of 1200 million (1.2 billion) total cells in subjects with ischemic stroke

-To determine the efficacy of MultiStem on stroke recovery in subjects with ischemic stroke.

Protection of trial subjects:

An Independent Safety Committee with multidisciplinary representation evaluated accumulating trial data and assessed the ongoing safety of the trial for the subjects enrolled. Following each data review, the Independent Safety Committee made a recommendation to the sponsor regarding continuation, revision of dosage, or termination of the trial.

The study was conducted in compliance with Good Clinical Practice, an international ethical and scientific quality standard for designing, conducting, recording, and reporting trials that involve human subjects. Compliance with this standard provides public assurance that the rights, safety, and well being of trial subjects are protected, consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical trial data are credible.

Background therapy: -

Evidence for comparator: -

|                                                           |                 |
|-----------------------------------------------------------|-----------------|
| Actual start date of recruitment                          | 24 October 2011 |
| Long term follow-up planned                               | No              |
| Independent data monitoring committee (IDMC) involvement? | Yes             |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United States: 131 |
| Country: Number of subjects enrolled | United Kingdom: 6  |
| Worldwide total number of subjects   | 137                |
| EEA total number of subjects         | 0                  |

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)                     | 80 |
| From 65 to 84 years                      | 57 |
| 85 years and over                        | 0  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Patients 18–79 years with a moderately severe ischaemic stroke with motor or speech deficit defined by a National Institutes of Health Stroke Scale (NIHSS) score of 8–20 at baseline just before administration ( $\geq 24$  h).

### Pre-assignment period milestones

|                            |     |
|----------------------------|-----|
| Number of subjects started | 137 |
|----------------------------|-----|

|                              |     |
|------------------------------|-----|
| Number of subjects completed | 134 |
|------------------------------|-----|

### Pre-assignment subject non-completion reasons

|                            |                                 |
|----------------------------|---------------------------------|
| Reason: Number of subjects | Consent withdrawn by subject: 3 |
|----------------------------|---------------------------------|

### Period 1

|                |                                |
|----------------|--------------------------------|
| Period 1 title | Overall trial (overall period) |
|----------------|--------------------------------|

|                              |     |
|------------------------------|-----|
| Is this the baseline period? | Yes |
|------------------------------|-----|

|                   |                         |
|-------------------|-------------------------|
| Allocation method | Randomised - controlled |
|-------------------|-------------------------|

|               |              |
|---------------|--------------|
| Blinding used | Double blind |
|---------------|--------------|

|               |                                                               |
|---------------|---------------------------------------------------------------|
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |
|---------------|---------------------------------------------------------------|

### Arms

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

|                  |                  |
|------------------|------------------|
| <b>Arm title</b> | Cohort 1 Placebo |
|------------------|------------------|

Arm description: -

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

|                                        |         |
|----------------------------------------|---------|
| Investigational medicinal product name | Placebo |
|----------------------------------------|---------|

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

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

|                      |          |
|----------------------|----------|
| Pharmaceutical forms | Infusion |
|----------------------|----------|

|                          |                 |
|--------------------------|-----------------|
| Routes of administration | Intravenous use |
|--------------------------|-----------------|

Dosage and administration details:

Single intravenous placebo infusion

|                  |                            |
|------------------|----------------------------|
| <b>Arm title</b> | Cohort 1 400 million cells |
|------------------|----------------------------|

Arm description: -

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

|                                        |           |
|----------------------------------------|-----------|
| Investigational medicinal product name | MultiStem |
|----------------------------------------|-----------|

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

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

|                      |          |
|----------------------|----------|
| Pharmaceutical forms | Infusion |
|----------------------|----------|

|                          |                 |
|--------------------------|-----------------|
| Routes of administration | Intravenous use |
|--------------------------|-----------------|

Dosage and administration details:

400 million cells

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | Cohort 2/3 Placebo |
|------------------|--------------------|

Arm description: -

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

|                                                                                     |                              |
|-------------------------------------------------------------------------------------|------------------------------|
| Investigational medicinal product name                                              | Placebo                      |
| Investigational medicinal product code                                              |                              |
| Other name                                                                          |                              |
| Pharmaceutical forms                                                                | Infusion                     |
| Routes of administration                                                            | Intravenous use              |
| Dosage and administration details:<br>Single intravenous placebo infusion           |                              |
| <b>Arm title</b>                                                                    | Cohort 2/3 1.2 billion cells |
| Arm description: -                                                                  |                              |
| Arm type                                                                            | Experimental                 |
| Investigational medicinal product name                                              | MultiStem                    |
| Investigational medicinal product code                                              |                              |
| Other name                                                                          |                              |
| Pharmaceutical forms                                                                | Infusion                     |
| Routes of administration                                                            | Intravenous use              |
| Dosage and administration details:<br>1.2 billion cells single intravenous infusion |                              |

| <b>Number of subjects in period 1<sup>[1]</sup></b> | Cohort 1 Placebo | Cohort 1 400 million cells | Cohort 2/3 Placebo |
|-----------------------------------------------------|------------------|----------------------------|--------------------|
| Started                                             | 2                | 6                          | 61                 |
| Completed                                           | 2                | 6                          | 48                 |
| Not completed                                       | 0                | 0                          | 13                 |
| Adverse event, serious fatal                        | -                | -                          | 9                  |
| Consent withdrawn by subject                        | -                | -                          | -                  |
| Lost to follow-up                                   | -                | -                          | 4                  |

| <b>Number of subjects in period 1<sup>[1]</sup></b> | Cohort 2/3 1.2 billion cells |
|-----------------------------------------------------|------------------------------|
| Started                                             | 65                           |
| Completed                                           | 58                           |
| Not completed                                       | 7                            |
| Adverse event, serious fatal                        | 5                            |
| Consent withdrawn by subject                        | 1                            |
| Lost to follow-up                                   | 1                            |

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: Three subjects withdrew consent before receiving allocated intervention.

## Baseline characteristics

### Reporting groups

|                                |                              |
|--------------------------------|------------------------------|
| Reporting group title          | Cohort 1 Placebo             |
| Reporting group description: - |                              |
| Reporting group title          | Cohort 1 400 million cells   |
| Reporting group description: - |                              |
| Reporting group title          | Cohort 2/3 Placebo           |
| Reporting group description: - |                              |
| Reporting group title          | Cohort 2/3 1.2 billion cells |
| Reporting group description: - |                              |

| Reporting group values                            | Cohort 1 Placebo | Cohort 1 400 million cells | Cohort 2/3 Placebo |
|---------------------------------------------------|------------------|----------------------------|--------------------|
| Number of subjects                                | 2                | 6                          | 61                 |
| Age categorical                                   |                  |                            |                    |
| Units: Subjects                                   |                  |                            |                    |
| Adults (18-64 years)                              | 1                | 6                          | 33                 |
| From 65-84 years                                  | 1                | 0                          | 28                 |
| Gender categorical                                |                  |                            |                    |
| Units: Subjects                                   |                  |                            |                    |
| Female                                            | 1                | 1                          | 28                 |
| Male                                              | 1                | 5                          | 33                 |
| Patients with left hemisphere event               |                  |                            |                    |
| Units: Subjects                                   |                  |                            |                    |
| Yes                                               | 2                | 5                          | 36                 |
| No                                                | 0                | 1                          | 25                 |
| Patients treated with tPA                         |                  |                            |                    |
| Units: Subjects                                   |                  |                            |                    |
| Yes                                               | 1                | 0                          | 29                 |
| No                                                | 1                | 6                          | 32                 |
| Patients treated with endovascular thrombectomy   |                  |                            |                    |
| Units: Subjects                                   |                  |                            |                    |
| Yes                                               | 0                | 0                          | 12                 |
| No                                                | 2                | 6                          | 49                 |
| Both tPA and endovascular thrombectomy            |                  |                            |                    |
| Units: Subjects                                   |                  |                            |                    |
| Yes                                               | 0                | 0                          | 9                  |
| No                                                | 2                | 6                          | 52                 |
| Any reperfusion therapy (tPA, thrombectomy, both) |                  |                            |                    |
| Units: Subjects                                   |                  |                            |                    |
| Yes                                               | 1                | 0                          | 32                 |
| No                                                | 1                | 6                          | 29                 |
| NIHSS 8-12 at baseline                            |                  |                            |                    |
| Units: Subjects                                   |                  |                            |                    |
| Yes                                               | 1                | 3                          | 27                 |
| No                                                | 1                | 3                          | 34                 |

|                                                                                        |               |                |                |
|----------------------------------------------------------------------------------------|---------------|----------------|----------------|
| Infarct size<br>Units: millilitre(s)<br>arithmetic mean<br>standard deviation          | 9.3<br>± 1.1  | 55.8<br>± 27.1 | 50.9<br>± 41.3 |
| Mean NIHSS at baseline                                                                 |               |                |                |
| National Institutes of Health Stroke Scale Score                                       |               |                |                |
| Units: none<br>arithmetic mean<br>standard deviation                                   | 15.5<br>± 5.0 | 12.2<br>± 2.9  | 13.3<br>± 3.7  |
| Median NIHSS at baseline                                                               |               |                |                |
| National Institutes of Health Stroke Scale Score                                       |               |                |                |
| Units: none<br>median<br>full range (min-max)                                          | 13<br>9 to 19 | 12<br>9 to 17  | 13<br>8 to 20  |
| Symptom onset to drug infusion<br>Units: hour<br>arithmetic mean<br>standard deviation | 32.8<br>± 3.4 | 31.7<br>± 2.8  | 39.3<br>± 6.7  |

| <b>Reporting group values</b>                                        | Cohort 2/3 1.2 billion cells | Total |  |
|----------------------------------------------------------------------|------------------------------|-------|--|
| Number of subjects                                                   | 65                           | 134   |  |
| Age categorical<br>Units: Subjects                                   |                              |       |  |
| Adults (18-64 years)                                                 | 37                           | 77    |  |
| From 65-84 years                                                     | 28                           | 57    |  |
| Gender categorical<br>Units: Subjects                                |                              |       |  |
| Female                                                               | 30                           | 60    |  |
| Male                                                                 | 35                           | 74    |  |
| Patients with left hemisphere event<br>Units: Subjects               |                              |       |  |
| Yes                                                                  | 37                           | 80    |  |
| No                                                                   | 28                           | 54    |  |
| Patients treated with tPA<br>Units: Subjects                         |                              |       |  |
| Yes                                                                  | 29                           | 59    |  |
| No                                                                   | 36                           | 75    |  |
| Patients treated with endovascular thrombectomy<br>Units: Subjects   |                              |       |  |
| Yes                                                                  | 17                           | 29    |  |
| No                                                                   | 48                           | 105   |  |
| Both tPA and endovascular thrombectomy<br>Units: Subjects            |                              |       |  |
| Yes                                                                  | 8                            | 17    |  |
| No                                                                   | 57                           | 117   |  |
| Any reperfusion therapy (tPA, thrombectomy, both)<br>Units: Subjects |                              |       |  |
| Yes                                                                  | 38                           | 71    |  |
| No                                                                   | 27                           | 63    |  |

|                                                  |         |    |  |
|--------------------------------------------------|---------|----|--|
| NIHSS 8-12 at baseline                           |         |    |  |
| Units: Subjects                                  |         |    |  |
| Yes                                              | 29      | 60 |  |
| No                                               | 36      | 74 |  |
| Infarct size                                     |         |    |  |
| Units: millilitre(s)                             |         |    |  |
| arithmetic mean                                  | 43.7    | -  |  |
| standard deviation                               | ± 26.9  | -  |  |
| Mean NIHSS at baseline                           |         |    |  |
| National Institutes of Health Stroke Scale Score |         |    |  |
| Units: none                                      |         |    |  |
| arithmetic mean                                  | 13.4    | -  |  |
| standard deviation                               | ± 3.6   | -  |  |
| Median NIHSS at baseline                         |         |    |  |
| National Institutes of Health Stroke Scale Score |         |    |  |
| Units: none                                      |         |    |  |
| median                                           | 13      | -  |  |
| full range (min-max)                             | 8 to 20 | -  |  |
| Symptom onset to drug infusion                   |         |    |  |
| Units: hour                                      |         |    |  |
| arithmetic mean                                  | 37.2    | -  |  |
| standard deviation                               | ± 6.9   | -  |  |

## End points

### End points reporting groups

|                                                                                                                                                                         |                                                       |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|
| Reporting group title                                                                                                                                                   | Cohort 1 Placebo                                      |
| Reporting group description: -                                                                                                                                          |                                                       |
| Reporting group title                                                                                                                                                   | Cohort 1 400 million cells                            |
| Reporting group description: -                                                                                                                                          |                                                       |
| Reporting group title                                                                                                                                                   | Cohort 2/3 Placebo                                    |
| Reporting group description: -                                                                                                                                          |                                                       |
| Reporting group title                                                                                                                                                   | Cohort 2/3 1.2 billion cells                          |
| Reporting group description: -                                                                                                                                          |                                                       |
| Subject analysis set title                                                                                                                                              | Cohort 2/3 Placebo Excluding Dual Reperfusion Therapy |
| Subject analysis set type                                                                                                                                               | Sub-group analysis                                    |
| Subject analysis set description:<br>Cohort 2/3 Placebo excluding subjects who received both tPA and mechanical reperfusion therapy.                                    |                                                       |
| Subject analysis set title                                                                                                                                              | Cohort 2/3 Original Trial Protocol - MultiStem        |
| Subject analysis set type                                                                                                                                               | Sub-group analysis                                    |
| Subject analysis set description:<br>Subjects receiving MultiStem within 36 hours of symptom onset excluding subjects treated with both tPA and mechanical reperfusion. |                                                       |
| Subject analysis set title                                                                                                                                              | Cohort 2/3 Early Treatment - Placebo                  |
| Subject analysis set type                                                                                                                                               | Sub-group analysis                                    |
| Subject analysis set description:<br>Subjects treated with placebo < 36 hours after symptom onset.                                                                      |                                                       |
| Subject analysis set title                                                                                                                                              | Cohort 2/3 Early Treatment - MultiStem                |
| Subject analysis set type                                                                                                                                               | Sub-group analysis                                    |
| Subject analysis set description:<br>Subjects treated with MultiStem < 36 hours after symptom onset.                                                                    |                                                       |

### Primary: Global Stroke Recovery

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                          |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Global Stroke Recovery <sup>[1][2]</sup> |
| End point description:<br>The primary efficacy outcome was the multivariate global stroke recovery at day 90, which assesses global disability, neurological deficit, and activities of daily living and consists of mRS 2 or less; NIHSS total score improvement of 75% or more from baseline; and Barthel index of 95 or more in the multipotent adult progenitor cells treatment group, compared with the placebo treatment. The data from these three binary variables from each patient were analysed with an additive logistic regression model with the treatment group and baseline NIHSS score ( $\leq 12$ or $\geq 13$ ) as dependent variables. |                                          |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Primary                                  |
| End point timeframe:<br>Day 90                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                          |

#### Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Primary and secondary efficacy endpoints are reported for all subjects receiving investigational product at the target dose of 1.2 billion cells (or match placebo) - Cohorts 2 and 3 combined.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Primary and secondary efficacy endpoints are reported for all subjects receiving investigational product at the target dose of 1.2 billion cells (or match placebo) - Cohorts 2 and 3 combined.

| <b>End point values</b>          | Cohort 2/3 Placebo  | Cohort 2/3 1.2 billion cells | Cohort 2/3 Placebo Excluding Dual Reperfusion Therapy | Cohort 2/3 Original Trial Protocol - MultiStem |
|----------------------------------|---------------------|------------------------------|-------------------------------------------------------|------------------------------------------------|
| Subject group type               | Reporting group     | Reporting group              | Subject analysis set                                  | Subject analysis set                           |
| Number of subjects analysed      | 61                  | 65                           | 52                                                    | 27                                             |
| Units: Odds ratio                |                     |                              |                                                       |                                                |
| number (confidence interval 95%) | 1.08 (0.55 to 2.09) | 1.08 (0.55 to 2.09)          | 2.28 (0.98 to 5.30)                                   | 2.28 (0.98 to 5.30)                            |

| <b>End point values</b>          | Cohort 2/3 Early Treatment - Placebo | Cohort 2/3 Early Treatment - MultiStem |  |  |
|----------------------------------|--------------------------------------|----------------------------------------|--|--|
| Subject group type               | Subject analysis set                 | Subject analysis set                   |  |  |
| Number of subjects analysed      | 19                                   | 31                                     |  |  |
| Units: Odds ratio                |                                      |                                        |  |  |
| number (confidence interval 95%) | 2.07 (0.70 to 6.10)                  | 2.07 (0.70 to 6.10)                    |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Modified Rankin Scale $\leq 2$

|                 |                                               |
|-----------------|-----------------------------------------------|
| End point title | Modified Rankin Scale $\leq 2$ <sup>[3]</sup> |
|-----------------|-----------------------------------------------|

End point description:

Number of subjects obtaining mRS outcome of two or better at Day 90 assessment.

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

End point timeframe:

90 Days

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Primary and secondary efficacy endpoints are reported for all subjects receiving investigational product at the target dose of 1.2 billion cells (or match placebo) - Cohorts 2 and 3 combined.

| <b>End point values</b>     | Cohort 2/3 Placebo | Cohort 2/3 1.2 billion cells | Cohort 2/3 Placebo Excluding Dual Reperfusion Therapy | Cohort 2/3 Original Trial Protocol - MultiStem |
|-----------------------------|--------------------|------------------------------|-------------------------------------------------------|------------------------------------------------|
| Subject group type          | Reporting group    | Reporting group              | Subject analysis set                                  | Subject analysis set                           |
| Number of subjects analysed | 61                 | 65                           | 52                                                    | 27                                             |
| Units: Subjects             |                    |                              |                                                       |                                                |
| mRS $\leq 2$                | 22                 | 24                           | 16                                                    | 13                                             |

| <b>End point values</b>     | Cohort 2/3<br>Early<br>Treatment -<br>Placebo | Cohort 2/3<br>Early<br>Treatment -<br>MultiStem |  |  |
|-----------------------------|-----------------------------------------------|-------------------------------------------------|--|--|
| Subject group type          | Subject analysis set                          | Subject analysis set                            |  |  |
| Number of subjects analysed | 19                                            | 31                                              |  |  |
| Units: Subjects             |                                               |                                                 |  |  |
| mRS ≤ 2                     | 5                                             | 14                                              |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: NIHSS Improvement ≥ 75%

|                 |                                        |
|-----------------|----------------------------------------|
| End point title | NIHSS Improvement ≥ 75% <sup>[4]</sup> |
|-----------------|----------------------------------------|

End point description:

Number of subjects exhibiting 75% or greater improvement in NIHSS from baseline to Day 90 assessment.

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

End point timeframe:

90 days

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Primary and secondary efficacy endpoints are reported for all subjects receiving investigational product at the target dose of 1.2 billion cells (or match placebo) - Cohorts 2 and 3 combined.

| <b>End point values</b>     | Cohort 2/3<br>Placebo | Cohort 2/3 1.2<br>billion cells | Cohort 2/3<br>Placebo<br>Excluding Dual<br>Reperfusion<br>Therapy | Cohort 2/3<br>Original Trial<br>Protocol -<br>MultiStem |
|-----------------------------|-----------------------|---------------------------------|-------------------------------------------------------------------|---------------------------------------------------------|
| Subject group type          | Reporting group       | Reporting group                 | Subject analysis set                                              | Subject analysis set                                    |
| Number of subjects analysed | 61                    | 65                              | 52                                                                | 27                                                      |
| Units: Subjects             |                       |                                 |                                                                   |                                                         |
| NIHSS Improvement ≥ 75%     | 23                    | 26                              | 16                                                                | 14                                                      |

| <b>End point values</b>     | Cohort 2/3<br>Early<br>Treatment -<br>Placebo | Cohort 2/3<br>Early<br>Treatment -<br>MultiStem |  |  |
|-----------------------------|-----------------------------------------------|-------------------------------------------------|--|--|
| Subject group type          | Subject analysis set                          | Subject analysis set                            |  |  |
| Number of subjects analysed | 19                                            | 31                                              |  |  |
| Units: Subjects             |                                               |                                                 |  |  |
| NIHSS Improvement ≥ 75%     | 6                                             | 15                                              |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Barthel Index $\geq$ 95

|                        |                                                                 |
|------------------------|-----------------------------------------------------------------|
| End point title        | Barthel Index $\geq$ 95 <sup>[5]</sup>                          |
| End point description: | Number of subjects achieving Barthel Index $\geq$ 95 at day 90. |
| End point type         | Secondary                                                       |
| End point timeframe:   | 90 days                                                         |

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Primary and secondary efficacy endpoints are reported for all subjects receiving investigational product at the target dose of 1.2 billion cells (or match placebo) - Cohorts 2 and 3 combined.

| End point values            | Cohort 2/3 Placebo | Cohort 2/3 1.2 billion cells | Cohort 2/3 Placebo Excluding Dual Reperfusion Therapy | Cohort 2/3 Original Trial Protocol - MultiStem |
|-----------------------------|--------------------|------------------------------|-------------------------------------------------------|------------------------------------------------|
| Subject group type          | Reporting group    | Reporting group              | Subject analysis set                                  | Subject analysis set                           |
| Number of subjects analysed | 61                 | 65                           | 52                                                    | 27                                             |
| Units: Subjects             |                    |                              |                                                       |                                                |
| Barthel Index $\geq$ 95     | 27                 | 30                           | 20                                                    | 15                                             |

| End point values            | Cohort 2/3 Early Treatment - Placebo | Cohort 2/3 Early Treatment - MultiStem |  |  |
|-----------------------------|--------------------------------------|----------------------------------------|--|--|
| Subject group type          | Subject analysis set                 | Subject analysis set                   |  |  |
| Number of subjects analysed | 19                                   | 31                                     |  |  |
| Units: Subjects             |                                      |                                        |  |  |
| Barthel Index $\geq$ 95     | 8                                    | 18                                     |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: NIHSS $\leq$ 1 or $\geq$ 11 point improvement

|                        |                                                                                                                                   |
|------------------------|-----------------------------------------------------------------------------------------------------------------------------------|
| End point title        | NIHSS $\leq$ 1 or $\geq$ 11 point improvement <sup>[6]</sup>                                                                      |
| End point description: | Number of subjects achieving NIHSS $\leq$ 1 at day 90 or exhibiting $\geq$ 11 point improvement in NIHSS from baseline to day 90. |
| End point type         | Secondary                                                                                                                         |
| End point timeframe:   | 90 days                                                                                                                           |

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Primary and secondary efficacy endpoints are reported for all subjects receiving investigational product at the target dose of 1.2 billion cells (or match placebo) - Cohorts 2 and 3 combined.

| <b>End point values</b>                       | Cohort 2/3 Placebo | Cohort 2/3 1.2 billion cells | Cohort 2/3 Placebo Excluding Dual Reperfusion Therapy | Cohort 2/3 Original Trial Protocol - MultiStem |
|-----------------------------------------------|--------------------|------------------------------|-------------------------------------------------------|------------------------------------------------|
| Subject group type                            | Reporting group    | Reporting group              | Subject analysis set                                  | Subject analysis set                           |
| Number of subjects analysed                   | 61                 | 65                           | 52                                                    | 27                                             |
| Units: Subjects                               |                    |                              |                                                       |                                                |
| NIHSS $\leq 1$ or $\geq 11$ point improvement | 18                 | 25                           | 15                                                    | 12                                             |

### Statistical analyses

No statistical analyses for this end point

### Secondary: mRS $\leq 1$

|                        |                                                      |
|------------------------|------------------------------------------------------|
| End point title        | mRS $\leq 1$ <sup>[7]</sup>                          |
| End point description: | Number of subjects achieving mRS $\leq 1$ at day 90. |
| End point type         | Secondary                                            |
| End point timeframe:   | 90 days                                              |

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Primary and secondary efficacy endpoints are reported for all subjects receiving investigational product at the target dose of 1.2 billion cells (or match placebo) - Cohorts 2 and 3 combined.

| <b>End point values</b>     | Cohort 2/3 Placebo | Cohort 2/3 1.2 billion cells | Cohort 2/3 Placebo Excluding Dual Reperfusion Therapy | Cohort 2/3 Original Trial Protocol - MultiStem |
|-----------------------------|--------------------|------------------------------|-------------------------------------------------------|------------------------------------------------|
| Subject group type          | Reporting group    | Reporting group              | Subject analysis set                                  | Subject analysis set                           |
| Number of subjects analysed | 61                 | 65                           | 52                                                    | 27                                             |
| Units: Subjects             |                    |                              |                                                       |                                                |
| mRS $\leq 1$                | 7                  | 10                           | 3                                                     | 5                                              |

| <b>End point values</b>     | Cohort 2/3 Early Treatment - Placebo | Cohort 2/3 Early Treatment - MultiStem |  |  |
|-----------------------------|--------------------------------------|----------------------------------------|--|--|
| Subject group type          | Subject analysis set                 | Subject analysis set                   |  |  |
| Number of subjects analysed | 19                                   | 31                                     |  |  |
| Units: Subjects             |                                      |                                        |  |  |

|         |   |   |  |  |
|---------|---|---|--|--|
| mRS ≤ 1 | 1 | 5 |  |  |
|---------|---|---|--|--|

## Statistical analyses

No statistical analyses for this end point

### Secondary: NIHSS ≤ 1

|                 |                          |
|-----------------|--------------------------|
| End point title | NIHSS ≤ 1 <sup>[8]</sup> |
|-----------------|--------------------------|

End point description:

Number of subjects achieving NIHSS ≤ 1 at day 90.

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

End point timeframe:

90 days

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Primary and secondary efficacy endpoints are reported for all subjects receiving investigational product at the target dose of 1.2 billion cells (or match placebo) - Cohorts 2 and 3 combined.

| End point values            | Cohort 2/3 Placebo | Cohort 2/3 1.2 billion cells | Cohort 2/3 Placebo Excluding Dual Reperfusion Therapy | Cohort 2/3 Original Trial Protocol - MultiStem |
|-----------------------------|--------------------|------------------------------|-------------------------------------------------------|------------------------------------------------|
| Subject group type          | Reporting group    | Reporting group              | Subject analysis set                                  | Subject analysis set                           |
| Number of subjects analysed | 61                 | 65                           | 52                                                    | 27                                             |
| Units: Subjects             |                    |                              |                                                       |                                                |
| NIHSS ≤ 1                   | 10                 | 17                           | 8                                                     | 9                                              |

| End point values            | Cohort 2/3 Early Treatment - Placebo | Cohort 2/3 Early Treatment - MultiStem |  |  |
|-----------------------------|--------------------------------------|----------------------------------------|--|--|
| Subject group type          | Subject analysis set                 | Subject analysis set                   |  |  |
| Number of subjects analysed | 19                                   | 31                                     |  |  |
| Units: Subjects             |                                      |                                        |  |  |
| NIHSS ≤ 1                   | 5                                    | 10                                     |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Excellent outcome

|                 |                                  |
|-----------------|----------------------------------|
| End point title | Excellent outcome <sup>[9]</sup> |
|-----------------|----------------------------------|

End point description:

Number of subjects achieving Excellent Outcome. Defined as a composite of mRS  $\leq$  1, NIHSS  $\leq$  1, and Barthel Index  $\geq$  95.

End point type Secondary

End point timeframe:

90 days

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Primary and secondary efficacy endpoints are reported for all subjects receiving investigational product at the target dose of 1.2 billion cells (or match placebo) - Cohorts 2 and 3 combined.

| End point values            | Cohort 2/3 Placebo | Cohort 2/3 1.2 billion cells | Cohort 2/3 Placebo Excluding Dual Reperfusion Therapy | Cohort 2/3 Original Trial Protocol - MultiStem |
|-----------------------------|--------------------|------------------------------|-------------------------------------------------------|------------------------------------------------|
| Subject group type          | Reporting group    | Reporting group              | Subject analysis set                                  | Subject analysis set                           |
| Number of subjects analysed | 61                 | 65                           | 52                                                    | 27                                             |
| Units: Subjects             |                    |                              |                                                       |                                                |
| Excellent Outcome           | 4                  | 10                           | 2                                                     | 5                                              |

| End point values            | Cohort 2/3 Early Treatment - Placebo | Cohort 2/3 Early Treatment - MultiStem |  |  |
|-----------------------------|--------------------------------------|----------------------------------------|--|--|
| Subject group type          | Subject analysis set                 | Subject analysis set                   |  |  |
| Number of subjects analysed | 19                                   | 31                                     |  |  |
| Units: Subjects             |                                      |                                        |  |  |
| Excellent Outcome           | 0                                    | 5                                      |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Global Stroke Recovery

End point title Global Stroke Recovery<sup>[10]</sup>

End point description:

Multivariate global stroke recovery at 1 year, which assesses global disability, neurological deficit, and activities of daily living and consists of mRS 2 or less; NIHSS total score improvement of 75% or more from baseline; and Barthel index of 95 or more in the multipotent adult progenitor cells treatment group, compared with the placebo treatment.

The data from these three binary variables from each patient were analysed with an additive logistic regression model with the treatment group and baseline NIHSS score ( $\leq$ 12 or  $\geq$ 13) as dependent variables.

End point type Secondary

End point timeframe:

1 year

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Primary and secondary efficacy endpoints are reported for all subjects receiving investigational product at the target dose of 1.2 billion cells (or match placebo) - Cohorts 2 and 3 combined.

| <b>End point values</b>          | Cohort 2/3 Placebo  | Cohort 2/3 1.2 billion cells | Cohort 2/3 Placebo Excluding Dual Reperfusion Therapy | Cohort 2/3 Original Trial Protocol - MultiStem |
|----------------------------------|---------------------|------------------------------|-------------------------------------------------------|------------------------------------------------|
| Subject group type               | Reporting group     | Reporting group              | Subject analysis set                                  | Subject analysis set                           |
| Number of subjects analysed      | 61                  | 65                           | 52                                                    | 27                                             |
| Units: Odds ratio                |                     |                              |                                                       |                                                |
| number (confidence interval 95%) | 1.48 (0.77 to 2.84) | 1.48 (0.77 to 2.84)          | 1.84 (0.81 to 4.20)                                   | 1.84 (0.81 to 4.20)                            |

| <b>End point values</b>          | Cohort 2/3 Early Treatment - Placebo | Cohort 2/3 Early Treatment - MultiStem |  |  |
|----------------------------------|--------------------------------------|----------------------------------------|--|--|
| Subject group type               | Subject analysis set                 | Subject analysis set                   |  |  |
| Number of subjects analysed      | 19                                   | 31                                     |  |  |
| Units: Odds ratio                |                                      |                                        |  |  |
| number (confidence interval 95%) | 1.14 (0.38 to 3.43)                  | 1.14 (0.38 to 3.43)                    |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Modified Rankin Scale $\leq 2$

|                        |                                                                                 |
|------------------------|---------------------------------------------------------------------------------|
| End point title        | Modified Rankin Scale $\leq 2$ <sup>[11]</sup>                                  |
| End point description: | Number of subjects obtaining mRS outcome of two or better at 1 year assessment. |
| End point type         | Secondary                                                                       |
| End point timeframe:   | 1 year                                                                          |

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Primary and secondary efficacy endpoints are reported for all subjects receiving investigational product at the target dose of 1.2 billion cells (or match placebo) - Cohorts 2 and 3 combined.

| End point values            | Cohort 2/3 Placebo | Cohort 2/3 1.2 billion cells | Cohort 2/3 Placebo Excluding Dual Reperfusion Therapy | Cohort 2/3 Original Trial Protocol - MultiStem |
|-----------------------------|--------------------|------------------------------|-------------------------------------------------------|------------------------------------------------|
| Subject group type          | Reporting group    | Reporting group              | Subject analysis set                                  | Subject analysis set                           |
| Number of subjects analysed | 61                 | 65                           | 52                                                    | 27                                             |
| Units: Subjects             |                    |                              |                                                       |                                                |
| Modified Rankin Scale ≤ 2   | 27                 | 33                           | 20                                                    | 13                                             |

| End point values            | Cohort 2/3 Early Treatment - Placebo | Cohort 2/3 Early Treatment - MultiStem |  |  |
|-----------------------------|--------------------------------------|----------------------------------------|--|--|
| Subject group type          | Subject analysis set                 | Subject analysis set                   |  |  |
| Number of subjects analysed | 19                                   | 31                                     |  |  |
| Units: Subjects             |                                      |                                        |  |  |
| Modified Rankin Scale ≤ 2   | 10                                   | 15                                     |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: NIHSS Improvement ≥ 75%

End point title | NIHSS Improvement ≥ 75%<sup>[12]</sup>

End point description:

Number of subjects achieving NIHSS Improvement ≥ 75% from baseline to 1 year.

End point type | Secondary

End point timeframe:

1 year

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Primary and secondary efficacy endpoints are reported for all subjects receiving investigational product at the target dose of 1.2 billion cells (or match placebo) - Cohorts 2 and 3 combined.

| End point values            | Cohort 2/3 Placebo | Cohort 2/3 1.2 billion cells | Cohort 2/3 Placebo Excluding Dual Reperfusion Therapy | Cohort 2/3 Original Trial Protocol - MultiStem |
|-----------------------------|--------------------|------------------------------|-------------------------------------------------------|------------------------------------------------|
| Subject group type          | Reporting group    | Reporting group              | Subject analysis set                                  | Subject analysis set                           |
| Number of subjects analysed | 61                 | 65                           | 52                                                    | 27                                             |
| Units: Subjects             |                    |                              |                                                       |                                                |
| NIHSS Improvement ≥ 75%     | 28                 | 32                           | 23                                                    | 15                                             |

| <b>End point values</b>      | Cohort 2/3<br>Early<br>Treatment -<br>Placebo | Cohort 2/3<br>Early<br>Treatment -<br>MultiStem |  |  |
|------------------------------|-----------------------------------------------|-------------------------------------------------|--|--|
| Subject group type           | Subject analysis set                          | Subject analysis set                            |  |  |
| Number of subjects analysed  | 19                                            | 31                                              |  |  |
| Units: Subjects              |                                               |                                                 |  |  |
| NIHSS Improvement $\geq$ 75% | 10                                            | 16                                              |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Barthel Index $\geq$ 95

|                 |                                         |
|-----------------|-----------------------------------------|
| End point title | Barthel Index $\geq$ 95 <sup>[13]</sup> |
|-----------------|-----------------------------------------|

End point description:

Number of subjects achieving Barthel Index  $\geq$  95 at 1 year.

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

End point timeframe:

1 year

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Primary and secondary efficacy endpoints are reported for all subjects receiving investigational product at the target dose of 1.2 billion cells (or match placebo) - Cohorts 2 and 3 combined.

| <b>End point values</b>     | Cohort 2/3<br>Placebo | Cohort 2/3 1.2<br>billion cells | Cohort 2/3<br>Placebo<br>Excluding Dual<br>Reperfusion<br>Therapy | Cohort 2/3<br>Original Trial<br>Protocol -<br>MultiStem |
|-----------------------------|-----------------------|---------------------------------|-------------------------------------------------------------------|---------------------------------------------------------|
| Subject group type          | Reporting group       | Reporting group                 | Subject analysis set                                              | Subject analysis set                                    |
| Number of subjects analysed | 61                    | 65                              | 52                                                                | 27                                                      |
| Units: Subjects             |                       |                                 |                                                                   |                                                         |
| Barthel Index $\geq$ 95     | 27                    | 40                              | 22                                                                | 19                                                      |

| <b>End point values</b>     | Cohort 2/3<br>Early<br>Treatment -<br>Placebo | Cohort 2/3<br>Early<br>Treatment -<br>MultiStem |  |  |
|-----------------------------|-----------------------------------------------|-------------------------------------------------|--|--|
| Subject group type          | Subject analysis set                          | Subject analysis set                            |  |  |
| Number of subjects analysed | 19                                            | 31                                              |  |  |
| Units: Subjects             |                                               |                                                 |  |  |
| Barthel Index $\geq$ 95     | 10                                            | 21                                              |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: mRS $\leq$ 1

|                        |                                                                            |
|------------------------|----------------------------------------------------------------------------|
| End point title        | mRS $\leq$ 1 <sup>[14]</sup>                                               |
| End point description: | Number of subjects obtaining mRS outcome of $\leq$ 1 at 1 year assessment. |
| End point type         | Secondary                                                                  |
| End point timeframe:   | 1 year                                                                     |

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Primary and secondary efficacy endpoints are reported for all subjects receiving investigational product at the target dose of 1.2 billion cells (or match placebo) - Cohorts 2 and 3 combined.

| End point values            | Cohort 2/3 Placebo | Cohort 2/3 1.2 billion cells | Cohort 2/3 Placebo Excluding Dual Reperfusion Therapy | Cohort 2/3 Original Trial Protocol - MultiStem |
|-----------------------------|--------------------|------------------------------|-------------------------------------------------------|------------------------------------------------|
| Subject group type          | Reporting group    | Reporting group              | Subject analysis set                                  | Subject analysis set                           |
| Number of subjects analysed | 61                 | 65                           | 52                                                    | 27                                             |
| Units: Subjects             |                    |                              |                                                       |                                                |
| mRS $\leq$ 1                | 8                  | 18                           | 5                                                     | 9                                              |

| End point values            | Cohort 2/3 Early Treatment - Placebo | Cohort 2/3 Early Treatment - MultiStem |  |  |
|-----------------------------|--------------------------------------|----------------------------------------|--|--|
| Subject group type          | Subject analysis set                 | Subject analysis set                   |  |  |
| Number of subjects analysed | 19                                   | 31                                     |  |  |
| Units: Subjects             |                                      |                                        |  |  |
| mRS $\leq$ 1                | 2                                    | 10                                     |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: NIHSS $\leq$ 1

|                        |                                                        |
|------------------------|--------------------------------------------------------|
| End point title        | NIHSS $\leq$ 1 <sup>[15]</sup>                         |
| End point description: | Number of subjects achieving NIHSS $\leq$ 1 at 1 year. |
| End point type         | Secondary                                              |
| End point timeframe:   | 1 year                                                 |

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Primary and secondary efficacy endpoints are reported for all subjects receiving investigational product at the target dose of 1.2 billion cells (or match placebo) - Cohorts 2 and 3 combined.

| <b>End point values</b>     | Cohort 2/3 Placebo | Cohort 2/3 1.2 billion cells | Cohort 2/3 Placebo Excluding Dual Reperfusion Therapy | Cohort 2/3 Original Trial Protocol - MultiStem |
|-----------------------------|--------------------|------------------------------|-------------------------------------------------------|------------------------------------------------|
| Subject group type          | Reporting group    | Reporting group              | Subject analysis set                                  | Subject analysis set                           |
| Number of subjects analysed | 61                 | 65                           | 52                                                    | 27                                             |
| Units: Subjects             |                    |                              |                                                       |                                                |
| NIHSS $\leq$ 1              | 12                 | 19                           | 8                                                     | 10                                             |

| <b>End point values</b>     | Cohort 2/3 Early Treatment - Placebo | Cohort 2/3 Early Treatment - MultiStem |  |  |
|-----------------------------|--------------------------------------|----------------------------------------|--|--|
| Subject group type          | Subject analysis set                 | Subject analysis set                   |  |  |
| Number of subjects analysed | 19                                   | 31                                     |  |  |
| Units: Subjects             |                                      |                                        |  |  |
| NIHSS $\leq$ 1              | 4                                    | 11                                     |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Excellent outcome

End point title | Excellent outcome<sup>[16]</sup>

End point description:

Number of subjects achieving Excellent Outcome at 1 year. Defined as a composite of mRS  $\leq$  1, NIHSS  $\leq$  1, and Barthel Index  $\geq$  95.

End point type | Secondary

End point timeframe:

1 year

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Primary and secondary efficacy endpoints are reported for all subjects receiving investigational product at the target dose of 1.2 billion cells (or match placebo) - Cohorts 2 and 3 combined.

| <b>End point values</b>     | Cohort 2/3 Placebo | Cohort 2/3 1.2 billion cells | Cohort 2/3 Placebo Excluding Dual Reperfusion Therapy | Cohort 2/3 Original Trial Protocol - MultiStem |
|-----------------------------|--------------------|------------------------------|-------------------------------------------------------|------------------------------------------------|
| Subject group type          | Reporting group    | Reporting group              | Subject analysis set                                  | Subject analysis set                           |
| Number of subjects analysed | 61                 | 65                           | 52                                                    | 27                                             |
| Units: Subjects             |                    |                              |                                                       |                                                |
| Excellent outcome           | 5                  | 15                           | 3                                                     | 8                                              |

| <b>End point values</b>     | Cohort 2/3 Early Treatment - Placebo | Cohort 2/3 Early Treatment - MultiStem |  |  |
|-----------------------------|--------------------------------------|----------------------------------------|--|--|
| Subject group type          | Subject analysis set                 | Subject analysis set                   |  |  |
| Number of subjects analysed | 19                                   | 31                                     |  |  |
| Units: Subjects             |                                      |                                        |  |  |
| Excellent outcome           | 0                                    | 9                                      |  |  |

### **Statistical analyses**

No statistical analyses for this end point

## Adverse events

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

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Timeframe for reporting adverse events:

Through Day 365

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Adverse event reporting additional description:

There were no dose-limiting toxicity events in either group. There were no infusional or allergic reactions and no difference in treatment-emergent adverse events between the groups (64 [99%] of 65 patients in the multipotent adult progenitor cell group vs 59 [97%] of 61 in the placebo group).

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

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### Dictionary used

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

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|                    |      |
|--------------------|------|
| Dictionary version | 14.1 |
|--------------------|------|

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

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#### Notes:

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

Justification: Treatment-emergent adverse events (serious and non-serious) were not different between the multipotent adult progenitor cells and placebo arms. There was also no difference in the incidence of serious adverse events between the arms. Mortality was not different between the arms (5 [8%] patients died in the multipotent adult progenitor cell group vs 9 [15%] patients died in the placebo group;  $p=0.21$ ). See attached Lancet Neurology publication from 2017 for more details describing safety endpoints

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date         | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|--------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 26 July 2013 | In response to lower-than-expected enrolment rates in the early stages of the study, the protocol's inclusion and exclusion criteria were amended to broaden the eligible patient population: <ul style="list-style-type: none"><li data-bbox="418 443 1423 474">• The upper age limit was increased from 79 years to 83 years.</li><li data-bbox="418 474 1423 589">• The treatment window was expanded from 24–36 h to 24–48 h after stroke onset to better accommodate limited hours of operations of cell processing laboratories needed to prepare the investigational, first-generation MultiStem product configuration used in this study</li><li data-bbox="418 589 1423 678">• Allowed inclusion of patients receiving both tPA treatment and endovascular thrombectomy to accommodate evolving standards of care that included increasing use of endovascular thrombectomy following thrombolysis.</li></ul> |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/28320635>