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) 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 (≥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
Arm title	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

Arm title	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

Arm title	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:

Single intravenous placebo infusion

Arm title	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:

1.2 billion cells single intravenous infusion

Number of subjects in period 1[1]	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

Number of subjects in period 1[1]	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			
Units: millilitre(s)			
arithmetic mean	9.3	55.8	50.9
standard deviation	± 1.1	± 27.1	± 41.3
Mean NIHSS at baseline			
National Institutes of Health Stroke Scale Score			
Units: none			
arithmetic mean	15.5	12.2	13.3
standard deviation	± 5.0	± 2.9	± 3.7
Median NIHSS at baseline			
National Institutes of Health Stroke Scale Score			
Units: none			
median	13	12	13
full range (min-max)	9 to 19	9 to 17	8 to 20
Symptom onset to drug infusion			
Units: hour			
arithmetic mean	32.8	31.7	39.3
standard deviation	± 3.4	± 2.8	± 6.7

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

Primary: Global Stroke Recovery

End point title	Global Stroke Recovery[1][2]
End point description:	
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 (≤12 or ≥13) as dependent variables.	
End point type	Primary
End point timeframe:	
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.

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: 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)

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: 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 ≤ 2

End point title	Modified Rankin Scale ≤ 2[3]

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.

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 ≤ 2	22	24	16	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				
mRS ≤ 2	5	14		

Statistical analyses

No statistical analyses for this end point

Secondary: NIHSS Improvement ≥ 75%

End point title	NIHSS Improvement ≥ 75%[4]

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.

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%	23	26	16	14

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 Improvement ≥ 75%	6	15		

Statistical analyses

No statistical analyses for this end point

Secondary: Barthel Index ≥ 95

End point title	Barthel Index ≥ 95[5]

End point description:

Number of subjects achieving Barthel Index ≥ 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 ≥ 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 ≥ 95	8	18		

Statistical analyses

No statistical analyses for this end point

Secondary: NIHSS ≤ 1 or ≥ 11 point improvement

End point title	NIHSS ≤ 1 or ≥ 11 point improvement[6]

End point description:

Number of subjects achieving NIHSS ≤ 1 at day 90 or exhibiting ≥ 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.

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 or ≥ 11 point improvement	18	25	15	12

Statistical analyses

No statistical analyses for this end point

Secondary: mRS ≤ 1

End point title	mRS ≤ 1[7]

End point description:

Number of subjects achieving mRS ≤ 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.

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 ≤ 1	7	10	3	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				

mRS ≤ 1	1	5		

Statistical analyses

No statistical analyses for this end point

Secondary: NIHSS ≤ 1

End point title	NIHSS ≤ 1[8]

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[9]

End point description:

Number of subjects achieving Excellent Outcome. Defined as a composite of mRS ≤ 1, NIHSS ≤ 1, and Barthel Index ≥ 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[10]

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 (≤12 or ≥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.

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: 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)

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: 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 ≤ 2

End point title	Modified Rankin Scale ≤ 2[11]

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%[12]

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

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 Improvement ≥ 75%	10	16		

Statistical analyses

No statistical analyses for this end point

Secondary: Barthel Index ≥ 95

End point title	Barthel Index ≥ 95[13]

End point description:

Number of subjects achieving Barthel Index ≥ 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.

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 ≥ 95	27	40	22	19

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 ≥ 95	10	21		

Statistical analyses

No statistical analyses for this end point

Secondary: mRS ≤ 1

End point title	mRS ≤ 1[14]

End point description:

Number of subjects obtaining mRS outcome of ≤ 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 ≤ 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 ≤ 1	2	10		

Statistical analyses

No statistical analyses for this end point

Secondary: NIHSS ≤ 1

End point title	NIHSS ≤ 1[15]

End point description:

Number of subjects achieving NIHSS ≤ 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.

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	12	19	8	10

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	4	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Excellent outcome

End point title	Excellent outcome[16]

End point description:

Number of subjects achieving Excellent Outcome at 1 year. Defined as a composite of mRS ≤ 1, NIHSS ≤ 1, and Barthel Index ≥ 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.

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	5	15	3	8

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	9		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
Through Day 365	
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).	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.1

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

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: • The upper age limit was increased from 79 years to 83 years. • 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 • 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.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

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