



Clinical trial results: Subarachnoid administration of autologous bone marrow stromal cells in incomplete spinal cord injury.

Summary

EudraCT number	2011-005684-24
Trial protocol	ES
Global end of trial date	09 May 2016

Results information

Result version number	v1 (current)
This version publication date	19 February 2023
First version publication date	19 February 2023

Trial information

Trial identification

Sponsor protocol code	CME-LEM2
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02165904
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Fundación Investigación Biomédica Hospital Universitario Puerta de Hierro
Sponsor organisation address	C/ Joaquín Rodrigo, 2, Majadahonda (Madrid), Spain, 28222
Public contact	Site contact point , Fundación Investigación Biomédica Hospital Universitario Puerta de Hierro, +34 91 1917760,
Scientific contact	Site contact point, Fundación Investigación Biomédica Hospital Universitario Puerta de Hierro, +34 91 1917760,

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	06 September 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 May 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Analyze the possible clinical efficacy of the administration of autologous stromal cells from the bone marrow expanded "in vitro" in the treatment of spinal cord injury patients (SCI) chronically established and incomplete (ASIA B, C or D).

Protection of trial subjects:

Previous to NC1 preparation, a sample of peripheral blood was retrieved from each patient for genomic studies in order to rule out chromosomal abnormalities that could discourage cell expansion.

Background therapy:

Patients performed physical therapy exercises.

Evidence for comparator: -

Actual start date of recruitment	22 May 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 12
Worldwide total number of subjects	12
EEA total number of subjects	12

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)	12
From 65 to 84 years	0

85 years and over	0
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Subject disposition

Recruitment

Recruitment details:

The planned duration of the clinical trial was 24 months. The duration of the recruitment phase was 12 months, and the duration of the follow-up period after treatment was 12 months.

Pre-assignment

Screening details:

After signing the Informed Consent Form, participants were tested to determine if they met all the inclusion criteria and none of the exclusion criteria.

Pre-assignment period milestones

Number of subjects started	12
Number of subjects completed	10

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Default selection criteria: 2
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Period 1

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

Blinding implementation details:

Not applicable. All the participants received the same treatment.

Arms

Arm title	Arm 1
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Arm description:

Treatment arm

Arm type	Experimental
Investigational medicinal product name	NC1
Investigational medicinal product code	
Other name	PEI number 12-141 (by the Spanish Agency of Medicament and Health Products)
Pharmaceutical forms	Suspension for injection
Routes of administration	Intrathecal use

Dosage and administration details:

Administration inside of the syringe of four doses of 30×10^6 autologous expanded mesenchymal stromal cells, supported in autologous plasma, through a surgical approach to the spinal cord (months 1, 4, 7 and 10). Therefore each patient received a total of 120×10^6 mesenchymal stromal cells.

Number of subjects in period 1 ^[1]	Arm 1
Started	10
Completed	10

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: 12 patients were enrolled in the study, but 2 of them were screening failures and did not receive the study treatment.

Baseline characteristics

Reporting groups

Reporting group title	Overall trial (overall period)
Reporting group description: -	

Reporting group values	Overall trial (overall period)	Total	
Number of subjects	10	10	
Age categorical			
Age ranged between 34 and 59 years.			
Units: Subjects			
Adults (18-64 years)	10	10	
Age continuous			
Units: years			
arithmetic mean	42.90		
standard deviation	± 8.85	-	
Gender categorical			
Units: Subjects			
Female	2	2	
Male	8	8	
American Spinal Injury Association Impairment Scale (ASIA) grade			
Units: Subjects			
ASIA B	4	4	
ASIA C	5	5	
ASIA D	1	1	
Spinal cord injury (SCI) vertebral level			
Units: Subjects			
C3-C4	1	1	
C5-C5	1	1	
C5-C6	3	3	
D2	1	1	
D7-D8	1	1	
L1	2	2	
L1-L2	1	1	
Time since Spinal cord injury (SCI)			
Units: Subjects			
2.43	1	1	
3.60	1	1	
6.00	1	1	
8.17	1	1	
13.06	1	1	
14.31	1	1	
17.76	1	1	
20.90	1	1	
21.32	1	1	
34.59	1	1	

Time from spinal cord injury to treatment			
Units: years			
arithmetic mean	14.21		
standard deviation	± 9.88	-	

End points

End points reporting groups

Reporting group title	Arm 1
Reporting group description:	
Treatment arm	
Subject analysis set title	Before treatment
Subject analysis set type	Per protocol
Subject analysis set description:	
Baseline characteristics of the subjects	
Subject analysis set title	At 3 months follow-up
Subject analysis set type	Per protocol
Subject analysis set description:	
Characteristics of the subjects at 3 months follow-up	
Subject analysis set title	At 6 months follow-up
Subject analysis set type	Per protocol
Subject analysis set description:	
Characteristics of the subjects at 6 months follow-up	
Subject analysis set title	At 9 months follow-up
Subject analysis set type	Per protocol
Subject analysis set description:	
Characteristics of the subjects at 9 months follow-up	
Subject analysis set title	At 12 months follow-up
Subject analysis set type	Per protocol
Subject analysis set description:	
Characteristics of the subjects at 12 months follow-up	
Subject analysis set title	At 4 months follow-up
Subject analysis set type	Per protocol
Subject analysis set description:	
Characteristics of the subjects at 4 months follow-up	
Subject analysis set title	At 7 months follow-up
Subject analysis set type	Per protocol
Subject analysis set description:	
Characteristics of the subjects at 7 months follow-up	
Subject analysis set title	At 10 months follow-up
Subject analysis set type	Per protocol
Subject analysis set description:	
Characteristics of the subjects at 10 months follow-up	

Primary: Change in the score in ASIA scale

End point title	Change in the score in ASIA scale
End point description:	
ASIA scale was used for sensitivity and motor assessments. Efficacy was assessed by taking into account the variation in the scores in the different scales between the subject's inclusion in the study and the scores obtained at the end of the follow-up period. A minimum possible score is 0 points. A maximum possible score is 224 points for a patient with normal sensation.	
End point type	Primary
End point timeframe:	
Measure before treatment (baseline visit), 3, 6, 9 and 12 months after surgery	

End point values	Before treatment	At 3 months follow-up	At 6 months follow-up	At 9 months follow-up
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	10	10	10
Units: Score				
arithmetic mean (standard deviation)				
Total Score	188.2 (± 60)	202.2 (± 63.7)	218.4 (± 57.5)	228.9 (± 51.84)
Pin Prick Score	54.50 (± 34.36)	61.20 (± 37.42)	71.60 (± 31.96)	78.30 (± 27.33)
Light Touch Score	80.70 (± 11.70)	85.40 (± 14.08)	89.10 (± 13.19)	92.00 (± 13.26)
Motor Score	53.00 (± 20.45)	55.60 (± 21.45)	57.70 (± 21.15)	58.60 (± 20.83)

End point values	At 12 months follow-up			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: Score				
arithmetic mean (standard deviation)				
Total Score	235.5 (± 49.35)			
Pin Prick Score	82.80 (± 24.69)			
Light Touch Score	93.50 (± 12.89)			
Motor Score	59.20 (± 21.15)			

Statistical analyses

Statistical analysis title	Total Score: before treatment vs at 3 months FU
Comparison groups	Before treatment v At 3 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.005
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Total Score: before treatment vs at 6 months FU
Comparison groups	Before treatment v At 6 months follow-up

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.005
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Total Score: before treatment vs at 9 months FU
Comparison groups	Before treatment v At 9 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.005
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Total Score: before treatment vs at 12 months FU
Comparison groups	Before treatment v At 12 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.005
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	PinPrick Score: before treatment vs at 3 months FU
Comparison groups	Before treatment v At 3 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.028
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	PinPrick Score: before treatment vs at 6 months FU
Comparison groups	Before treatment v At 6 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.008
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	PinPrick Score: before treatment vs at 9 months FU
Comparison groups	Before treatment v At 9 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.008
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	PinPrick Score: before treatment vs at 12 months
Comparison groups	Before treatment v At 12 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.005
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Light Touch Score: before treatment vs at 3 months
Comparison groups	Before treatment v At 3 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.01
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Light Touch Score: before treatment vs at 6 months
Comparison groups	Before treatment v At 6 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.005
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Light Touch Score: before treatment vs at 9 months
Comparison groups	Before treatment v At 9 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.005
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Light Touch Score: before treatment vs 12 months
Comparison groups	Before treatment v At 12 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.005
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Motor Score: before treatment vs at 3 months FU
Comparison groups	At 3 months follow-up v Before treatment
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.028
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Motor Score: before treatment vs at 6 months FU
Comparison groups	Before treatment v At 6 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.008
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Motor Score: before treatment vs at 9 months FU
Comparison groups	Before treatment v At 9 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.008
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Motor Score: before treatment vs at 12 months FU
Comparison groups	Before treatment v At 12 months follow-up

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.008
Method	Wilcoxon (Mann-Whitney)

Primary: Change in the score in NIF scale

End point title	Change in the score in NIF scale
End point description:	
Changes in Functional Independence Measure scale (NIF scale), score at the beginning, through and the end of the treatment.	
Ranges score: 18 to 126. Being 18 total patient dependency and 126 total patient independence.	
End point type	Primary
End point timeframe:	
Measure before treatment (baseline visit), 3, 6, 9 and 12 months after surgery	

End point values	Before treatment	At 3 months follow-up	At 6 months follow-up	At 9 months follow-up
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	10	10	10
Units: Score on a scale				
arithmetic mean (standard deviation)	95.7 (± 33.9)	95.7 (± 33.9)	95.7 (± 33.9)	96.10 (± 33.42)

End point values	At 12 months follow-up			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: Score on a scale				
arithmetic mean (standard deviation)	98.6 (± 32.05)			

Statistical analyses

Statistical analysis title	Before treatment v At 3 months follow-up
Comparison groups	Before treatment v At 3 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 1
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Before treatment v At 6 months follow-up
Comparison groups	Before treatment v At 6 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 1
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Before treatment v At 9 months follow-up
Comparison groups	Before treatment v At 9 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.157
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Before treatment v At 12 months follow-up
Comparison groups	Before treatment v At 12 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.027
Method	Wilcoxon (Mann-Whitney)

Primary: Change in the score in BARTHEL Scale

End point title	Change in the score in BARTHEL Scale
End point description:	
Changes in Barthel score at the beginning, through and the end of the treatment.	
Ranges score: 0 to 100. Being 0 total patient dependency and 100 total patient independence.	
End point type	Primary
End point timeframe:	
Measure before treatment (baseline visit), 3, 6,9 and 12 months after surgery	

End point values	Before treatment	At 3 months follow-up	At 6 months follow-up	At 9 months follow-up
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	10	10	10
Units: Score on a scale				
arithmetic mean (standard deviation)	58 (\pm 36.07)	58 (\pm 36.07)	58 (\pm 36.07)	58 (\pm 36.07)

End point values	At 12 months follow-up			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: Score on a scale				
arithmetic mean (standard deviation)	65 (\pm 35.59)			

Statistical analyses

Statistical analysis title	Before treatment v At 3 months follow-up
Comparison groups	Before treatment v At 3 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 1
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Before treatment v At 6 months follow-up
Comparison groups	Before treatment v At 6 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 1
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Before treatment v At 9 months follow-up
Comparison groups	Before treatment v At 9 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 1
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Before treatment v At 12 months follow-up
Comparison groups	Before treatment v At 12 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.039
Method	Wilcoxon (Mann-Whitney)

Primary: Change in the score in IANR-SCIFRS scale

End point title	Change in the score in IANR-SCIFRS scale
End point description: Changes in IANR-SCIFRS scale. The SCI Functional Rating Scale of the International Association of Neurorestoratology scale. This scale evaluates the global spinal cord function through nine sections, with a final section that only applies to men and assesses sexual function. Ranges score: 0 to 48. Being 0 severe degree of disability and 48 normal value.	
End point type	Primary
End point timeframe: Changes in IANR-SCIFRS scale before surgery (baseline visit) and 3, 6, 9, 12 months after surgery (follow-up period)	

End point values	Before treatment	At 3 months follow-up	At 6 months follow-up	At 9 months follow-up
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	10	10	10
Units: Score on a scale				
arithmetic mean (standard deviation)				
Global	29.10 (± 9.96)	31.5 (± 8.9)	33.9 (± 9.73)	35.9 (± 9.01)
Sexual (male)	1.88 (± 0.64)	1.88 (± 0.64)	2.13 (± 0.64)	2.13 (± 0.64)

End point values	At 12 months follow-up			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: Score on a scale				
arithmetic mean (standard deviation)				
Global	36.9 (± 8.21)			
Sexual (male)	2.13 (± 0.64)			

Statistical analyses

Statistical analysis title	Global: Before treatment v At 3 months follow-up
Comparison groups	At 3 months follow-up v Before treatment

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.017
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Global: Before treatment v At 6 months follow-up
Comparison groups	Before treatment v At 6 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.005
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Global: Before treatment v At 9 months follow-up
Comparison groups	Before treatment v At 9 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.005
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Global: Before treatment v At 12 months follow-up
Comparison groups	Before treatment v At 12 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.005
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Sexual Score (M): before treatment vs at 3 months
Comparison groups	Before treatment v At 3 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 1
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Sexual Score (M): before treatment vs at 6 months
Comparison groups	Before treatment v At 6 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.157
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Sexual Score (M): before treatment vs at 9 months
Comparison groups	Before treatment v At 9 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.157
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Sexual Score (M): before treatment vs at 12 months
Comparison groups	Before treatment v At 12 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.157
Method	Wilcoxon (Mann-Whitney)

Primary: Change in the score in PENN scale

End point title	Change in the score in PENN scale
End point description:	
PENN scale measures the degree of spasms. Changes in PENN score at the beginning, through and the end of the treatment	
Ranges score: 0 to 4. Being 0 absence of spasms and 4 frequency greater than 10 spasms per hour.	
End point type	Primary
End point timeframe:	
Measure before treatment (baseline visit), 3, 6, 9 and 12 months after surgery	

End point values	Before treatment	At 3 months follow-up	At 6 months follow-up	At 9 months follow-up
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	10	10	10
Units: Score on a scale				
arithmetic mean (standard deviation)	1.20 (± 1.14)	1.10 (± 1.10)	0.90 (± 0.88)	0.90 (± 0.88)

End point values	At 12 months follow-up			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: Score on a scale				
arithmetic mean (standard deviation)	0.90 (\pm 0.88)			

Statistical analyses

Statistical analysis title	Before treatment v At 3 months follow-up
Comparison groups	Before treatment v At 3 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.317
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Before treatment v At 6 months follow-up
Comparison groups	Before treatment v At 6 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.18
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Before treatment v At 9 months follow-up
Comparison groups	Before treatment v At 9 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.18
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Before treatment v At 12 months follow-up
Comparison groups	Before treatment v At 12 months follow-up

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.18
Method	Wilcoxon (Mann-Whitney)

Primary: Change in the score in Ashworth scale

End point title	Change in the score in Ashworth scale
End point description:	
Ashworth scale measures the degree of spasticity.	
Efficacy was assessed by taking into account the variation in ASHWORTH score at the beginning, through and the end of the treatment	
Ranges score: 0 to 4. Being 0 when there isn't increase in muscle tone when stretching, and 4 when there is rigid affected follow-up in flexion or extension	
End point type	Primary
End point timeframe:	
Measure before treatment (baseline visit), 3, 6,9 and 12 months after surgery	

End point values	Before treatment	At 3 months follow-up	At 6 months follow-up	At 9 months follow-up
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	10	10	10
Units: Score on scale				
arithmetic mean (standard deviation)	1.4 (± 0.81)	1.4 (± 0.81)	1.4 (± 0.81)	1.4 (± 0.81)

End point values	At 12 months follow-up			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: Score on scale				
arithmetic mean (standard deviation)	1.10 (± 0.99)			

Statistical analyses

Statistical analysis title	before treatment vs at 3 months FU
Comparison groups	Before treatment v At 3 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 1
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	before treatment vs at 6 months FU
Comparison groups	Before treatment v At 6 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 1
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	before treatment vs at 9 months FU
Comparison groups	Before treatment v At 9 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 1
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	before treatment vs at 12 months FU
Comparison groups	Before treatment v At 12 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.157
Method	Wilcoxon (Mann-Whitney)

Primary: Change in score in VAS scale

End point title	Change in score in VAS scale
End point description: VAS: Visual Analog Scale. This scale evaluates neuropathic pain. Changes in VAS score at the beginning, through and the end of the treatment Ranges score: 0 to 10. Being 0 absence of pain and 10 the worst pain.	
End point type	Primary
End point timeframe: Measure before treatment (baseline visit), 3, 6,9 and 12 months after surgery	

End point values	Before treatment	At 3 months follow-up	At 6 months follow-up	At 9 months follow-up
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	10	10	10
Units: Score on a scale				
arithmetic mean (standard deviation)	1.70 (± 3.13)	0.70 (± 1.16)	0.60 (± 0.97)	0.40 (± 0.84)

End point values	At 12 months follow-up			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: Score on a scale				
arithmetic mean (standard deviation)	0.40 (± 0.84)			

Statistical analyses

Statistical analysis title	before treatment vs at 3 months FU
Comparison groups	Before treatment v At 3 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.109
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	before treatment vs at 6 months FU
Comparison groups	Before treatment v At 6 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.109
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	before treatment vs at 9 months FU
Comparison groups	Before treatment v At 9 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.109
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	before treatment vs at 12 months FU
Comparison groups	Before treatment v At 12 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.109
Method	Wilcoxon (Mann-Whitney)

Primary: Change in score in GEFNER scale

End point title	Change in score in GEFNER scale
End point description: Geffner scale was used for the study of bladder function. Efficacy was assessed by taking into account the variation in Geffner score before surgery (baseline visit) and 3, 6, 9, 12 months after surgery (follow-up period) Ranges score: 0 to 6. Being 0 absence of bladder control and 6 total control of bladder	
End point type	Primary
End point timeframe: Changes in Geffner scale before surgery (baseline visit) and 3, 6, 9, 12 months after surgery (follow-up period)	

End point values	Before treatment	At 3 months follow-up	At 6 months follow-up	At 9 months follow-up
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	10	10	10
Units: Score on scale				
arithmetic mean (standard deviation)	3.30 (± 1.34)	3.60 (± 1.26)	3.80 (± 1.14)	3.90 (± 1.10)

End point values	At 12 months follow-up			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: Score on scale				
arithmetic mean (standard deviation)	4.20 (± 1.23)			

Statistical analyses

Statistical analysis title	Before treatment v At 3 months follow-up
Comparison groups	Before treatment v At 3 months follow-up

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.18
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Before treatment v At 6 months follow-up
Comparison groups	At 6 months follow-up v Before treatment
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.102
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Before treatment v At 9 months follow-up
Comparison groups	Before treatment v At 9 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.063
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Before treatment v At 12 months follow-up
Comparison groups	Before treatment v At 12 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.024
Method	Wilcoxon (Mann-Whitney)

Primary: Change in score in NBD scale

End point title	Change in score in NBD scale
End point description: NBD scale was used for the study of of neurogenic bowel dysfunction (NBD). Efficacy was assessed by taking into account the variation in NBD score before surgery (baseline visit) and 3, 6, 9, 12 months after surgery (follow-up period) Ranges score: 0 to 47. 0-6 is very minor dysfunction. 7-9 is minor dysfunction. 10-13 is moderate dysfunction; and 14 or more is severe dysfunction.	
End point type	Primary
End point timeframe: Measure before treatment (baseline visit), 3, 6,9 and 12 months after surgery	

End point values	Before treatment	At 3 months follow-up	At 6 months follow-up	At 9 months follow-up
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	10	10	10
Units: Score on a scale				
arithmetic mean (standard deviation)	10.60 (± 6.64)	6.10 (± 4.15)	5.70 (± 4.35)	4.40 (± 3.86)

End point values	At 12 months follow-up			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: Score on a scale				
arithmetic mean (standard deviation)	4.20 (± 3.88)			

Statistical analyses

Statistical analysis title	Before treatment v At 3 months follow-up
Comparison groups	Before treatment v At 3 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.042
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Before treatment v At 6 months follow-up
Comparison groups	Before treatment v At 6 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.018
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Before treatment v At 9 months follow-up
Comparison groups	Before treatment v At 9 months follow-up

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.018
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Before treatment v At 12 months follow-up
Comparison groups	Before treatment v At 12 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.018
Method	Wilcoxon (Mann-Whitney)

Primary: Change in urodynamic studies: detrusor pressure	
End point title	Change in urodynamic studies: detrusor pressure
End point description: Urodynamic studies in terms of detrusor pressure (decrease on detrusor pressure is considered a clinical improvement)	
End point type	Primary
End point timeframe: Urodynamic studies before surgery, and at 6 and 12 months after surgery (follow-up)	

End point values	Before treatment	At 6 months follow-up	At 12 months follow-up	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	10	10	
Units: cm/H2O				
arithmetic mean (standard deviation)	68.6 (± 20.08)	53.8 (± 20.8)	51.5 (± 37.22)	

Statistical analyses

Statistical analysis title	Before treatment v At 6 months follow-up
Comparison groups	Before treatment v At 6 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.074
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Before treatment v At 12 months follow-up
Comparison groups	Before treatment v At 12 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.169
Method	Wilcoxon (Mann-Whitney)

Primary: Change in urodynamic studies: Bladder compliance

End point title	Change in urodynamic studies: Bladder compliance
End point description:	
Urodynamic studies in terms of Bladder compliance. Bladder compliance is the result of a mathematical calculation of volume responsible for 1 cm H2O pressure rise measured during a cystometric filling. It gives an indication on how the different mechanisms in the bladder wall react on stretching. It is obvious that compliance figures can vary widely in groups which makes it difficult to define limits of normality.	
End point type	Primary
End point timeframe:	
Measure before treatment (baseline visit), 6 and 12 months after surgery	

End point values	Before treatment	At 6 months follow-up	At 12 months follow-up	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	10	10	
Units: mL/cm H2O				
arithmetic mean (standard deviation)	3.88 (± 3.24)	6.14 (± 3.36)	8.28 (± 6.41)	

Statistical analyses

Statistical analysis title	Before treatment v At 6 months follow-up
Comparison groups	Before treatment v At 6 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.059
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Before treatment v At 12 months follow-up
Comparison groups	Before treatment v At 12 months follow-up

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.037
Method	Wilcoxon (Mann-Whitney)

Primary: Change in urodynamic studies: Maximum cystometric capacity

End point title	Change in urodynamic studies: Maximum cystometric capacity
End point description:	
Urodynamic studies in terms of Maximum cystometric capacity	
End point type	Primary
End point timeframe:	
Urodynamic studies before surgery, and at 6 and 12 months after surgery (follow-up)	

End point values	Before treatment	At 6 months follow-up	At 12 months follow-up	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	10	10	
Units: mL				
arithmetic mean (standard deviation)	234.9 (± 156.26)	292.4 (± 110.93)	292.6 (± 183.6)	

Statistical analyses

Statistical analysis title	Before treatment v At 6 months follow-up
Comparison groups	Before treatment v At 6 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.202
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Before treatment v At 12 months follow-up
Comparison groups	Before treatment v At 12 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.646
Method	Wilcoxon (Mann-Whitney)

Primary: Change in neurophysiological parameters: improvement in Somatosensory Evoked Potentials (SSEP)

End point title	Change in neurophysiological parameters: improvement in Somatosensory Evoked Potentials (SSEP)
End point description: Change in neurophysiological parameters: improvement in Somatosensory Evoked Potentials (SSEP)	
End point type	Primary
End point timeframe: Efficacy-measure before treatment (baseline visit), 6, and 12 months after surgery	

End point values	Before treatment	At 6 months follow-up	At 12 months follow-up	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	10	10	
Units: Number of patients				
Improvement in SSEP	0	7	8	
No improvement in SSEP	10	3	2	

Statistical analyses

Statistical analysis title	Before treatment vs at 6 months FU
Comparison groups	Before treatment v At 6 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.206
Method	Chi-squared

Statistical analysis title	Before treatment vs at 12 months FU
Comparison groups	Before treatment v At 12 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.058
Method	Chi-squared

Primary: Change in neurophysiological parameters: improvement in Motor Evoked Potentials (MEP)

End point title	Change in neurophysiological parameters: improvement in
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End point description:

Change in neurophysiological parameters: improvement in Motor Evoked Potentials (MEP)

End point type

Primary

End point timeframe:

Efficacy-measure before treatment (baseline visit), 6, and 12 months after surgery

End point values	Before treatment	At 6 months follow-up	At 12 months follow-up	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	10	10	
Units: Number of patients				
Improvement in MEP	0	4	5	
No improvement in MEP	10	6	5	

Statistical analyses

Statistical analysis title	Before treatment vs at 6 months FU
Comparison groups	Before treatment v At 6 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.4
Method	Chi-squared

Statistical analysis title	Before treatment vs at 12 months FU
Comparison groups	Before treatment v At 12 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 1
Method	Chi-squared

Primary: Change in neurophysiological parameters: improvement in sensitivity conduction

End point title

Change in neurophysiological parameters: improvement in sensitivity conduction

End point description:

Change in neurophysiological parameters: improvement in sensitivity conduction

End point type

Primary

End point timeframe:

Efficacy-measure before treatment (baseline visit), 6, and 12 months after surgery

End point values	Before treatment	At 6 months follow-up	At 12 months follow-up	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	10	10	
Units: Number of patients				
Improvement	0	2	3	
No improvement	10	8	7	

Statistical analyses

Statistical analysis title	Before treatment vs at 6 months FU
Comparison groups	Before treatment v At 6 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.058
Method	Chi-squared

Statistical analysis title	Before treatment vs at 12 months FU
Comparison groups	Before treatment v At 12 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.206
Method	Chi-squared

Primary: Change in neurophysiological parameters: improvement in motor conduction

End point title	Change in neurophysiological parameters: improvement in motor conduction
End point description:	Change in neurophysiological parameters: improvement in motor conduction
End point type	Primary
End point timeframe:	Efficacy-measure before treatment (baseline visit), 6, and 12 months after surgery

End point values	Before treatment	At 6 months follow-up	At 12 months follow-up	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	10	10	
Units: Number of patients				
Improvement	0	5	7	
No improvement	10	5	3	

Statistical analyses

Statistical analysis title	Before treatment vs at 6 months FU
Comparison groups	Before treatment v At 6 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 1
Method	Chi-squared

Statistical analysis title	Before treatment vs at 12 months FU
Comparison groups	Before treatment v At 12 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.206
Method	Chi-squared

Primary: Change in neurophysiological parameters: improvement in voluntary muscle contraction

End point title	Change in neurophysiological parameters: improvement in voluntary muscle contraction
End point description:	Change in neurophysiological parameters: improvement in voluntary muscle contraction
End point type	Primary
End point timeframe:	Efficacy-measure before treatment (baseline visit), 6, and 12 months after surgery

End point values	Before treatment	At 6 months follow-up	At 12 months follow-up	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	10	10	
Units: Number of patients				
Improvement	0	4	6	
No improvement	10	6	4	

Statistical analyses

Statistical analysis title	Before treatment vs at 6 months FU
Comparison groups	Before treatment v At 6 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.4
Method	Chi-squared

Statistical analysis title	Before treatment vs at 12 months FU
Comparison groups	Before treatment v At 12 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.4
Method	Chi-squared

Primary: Change in neurophysiological parameters: presence of infralesional activity muscle reinnervation

End point title	Change in neurophysiological parameters: presence of infralesional activity muscle reinnervation
End point description:	Change in neurophysiological parameters: presence of infralesional activity muscle reinnervation
End point type	Primary
End point timeframe:	Efficacy-measure before treatment (baseline visit), 6, and 12 months after surgery

End point values	Before treatment	At 6 months follow-up	At 12 months follow-up	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	10	10	
Units: Number of patients				
Improvement	0	7	9	
No improvement	10	3	1	

Statistical analyses

Statistical analysis title	Before treatment vs at 6 months FU
Comparison groups	Before treatment v At 6 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.206
Method	Chi-squared

Statistical analysis title	Before treatment vs at 12 months FU
Comparison groups	Before treatment v At 12 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.011
Method	Chi-squared

Primary: Modification of magnetic resonance imaging (MRI)

End point title	Modification of magnetic resonance imaging (MRI) ^[1]
End point description:	
Number of patients with changes in morphology of injury compared with basal images.	
End point type	Primary
End point timeframe:	
Before treatment (baseline visit) and at 12 months.	

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: A qualitative evaluation was performed, comparing the results at month 12 with the baseline values.

End point values	Before treatment	At 12 months follow-up		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	10		
Units: Number of patients				
Morphological changes	0	0		
No morphological changes	10	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in expression of neurotrophins (BDNF) in CSF (cerebrospinal fluid) samples

End point title	Change in expression of neurotrophins (BDNF) in CSF (cerebrospinal fluid) samples
End point description:	Changes in expression of neurotrophins in CSF (CerebroSpinal Fluid) samples obtained previously to first administration of cell therapy, and previously to the last administration, at month 10, in order to study the variability in the expression of neurotrophins along time. The mean+SD (standard deviation) at each time point was obtained. The tested neurotrophin was: BDNF (brain-derived neurotrophic factor).
End point type	Secondary
End point timeframe:	Basal and 10 months after the administration

End point values	Before treatment	At 10 months follow-up		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	9 ^[2]	9 ^[3]		
Units: pg/ml				
arithmetic mean (standard deviation)	19.14 (± 4.58)	33.82 (± 49.65)		

Notes:

[2] - This data was not obtained in one of the patients.

[3] - This data was not obtained in one of the patients.

Statistical analyses

Statistical analysis title	before treatment vs at 10 months FU
Comparison groups	Before treatment v At 10 months follow-up
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.515
Method	Wilcoxon (Mann-Whitney)

Secondary: Change in expression of neurotrophins (GDNF) in CSF (cerebrospinal fluid) samples

End point title	Change in expression of neurotrophins (GDNF) in CSF (cerebrospinal fluid) samples
End point description: Changes in expression of neurotrophins in CSF (CerebroSpinal Fluid) samples obtained previously to first administration of cell therapy, and previously to the last administration, at month 10, in order to study the variability in the expression of neurotrophins along time. The mean+SD (standard deviation) at each time point was obtained. The tested neurotrophin was: GDNF (glial cell line-derived neurotrophic factor).	
End point type	Secondary
End point timeframe: Basal, 4, 7 and 10 months after the administration	

End point values	Before treatment	At 4 months follow-up	At 7 months follow-up	At 10 months follow-up
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	10	8 ^[4]	10
Units: pg/ml				
arithmetic mean (standard deviation)	10.20 (± 1.96)	10.93 (± 2.37)	11.31 (± 1.57)	10.46 (± 2.79)

Notes:

[4] - This data was not obtained in two patients.

Statistical analyses

Statistical analysis title	before treatment vs at 4 months FU
Comparison groups	Before treatment v At 4 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.262
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	before treatment vs at 7 months FU
Comparison groups	Before treatment v At 7 months follow-up
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.398
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	before treatment vs at 10 months FU
Comparison groups	Before treatment v At 10 months follow-up

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.766
Method	Wilcoxon (Mann-Whitney)

Secondary: Change in expression of neurotrophins (NGF) in CSF (cerebrospinal fluid) samples

End point title	Change in expression of neurotrophins (NGF) in CSF (cerebrospinal fluid) samples
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End point description:

Changes in expression of neurotrophins in CSF (CerebroSpinal Fluid) samples obtained previously to first administration of cell therapy, and previously to the last administration, at month 10, in order to study the variability in the expression of neurotrophins along time. The mean+SD (standard deviation) at each time point was obtained. The tested neurotrophin was: NGF (nerve growth factor).

End point type	Secondary
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End point timeframe:

Basal 4, 7 and 10 months after the administration

End point values	Before treatment	At 4 months follow-up	At 7 months follow-up	At 10 months follow-up
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	10	8 ^[5]	10
Units: pg/ml				
arithmetic mean (standard deviation)	98.34 (± 19.34)	98.26 (± 17.30)	92.79 (± 12.01)	92.42 (± 14.84)

Notes:

[5] - This data was not obtained in two patients.

Statistical analyses

Statistical analysis title	before treatment vs at 4 months FU
Comparison groups	Before treatment v At 4 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.508
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	before treatment vs at 7 months FU
Comparison groups	Before treatment v At 7 months follow-up

Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.123
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	before treatment vs at 10 months FU
Comparison groups	Before treatment v At 10 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.575
Method	Wilcoxon (Mann-Whitney)

Secondary: Change in expression of neurotrophins (CNTF) in CSF (cerebrospinal fluid) samples

End point title	Change in expression of neurotrophins (CNTF) in CSF (cerebrospinal fluid) samples
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End point description:

Changes in expression of neurotrophins in CSF (CerebroSpinal Fluid) samples obtained previously to first administration of cell therapy, and previously to the last administration, at month 10, in order to study the variability in the expression of neurotrophins along time. The mean+SD (standard deviation) at each time point was obtained. The tested neurotrophin was: CNTF (Ciliary neurotrophic factor).

End point type	Secondary
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End point timeframe:

Basal 4,7 and 10 months after the administration

End point values	Before treatment	At 4 months follow-up	At 7 months follow-up	At 10 months follow-up
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	10	9 ^[6]	9 ^[7]
Units: pg/ml				
arithmetic mean (standard deviation)	5.82 (± 3.47)	6.66 (± 4.55)	8.76 (± 5.21)	7.73 (± 4.82)

Notes:

[6] - This data was not obtained in one of the patients.

[7] - This data was not obtained in one of the patients.

Statistical analyses

Statistical analysis title	before treatment vs at 4 months FU
Comparison groups	Before treatment v At 4 months follow-up

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.241
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	before treatment vs at 7 months FU
Comparison groups	Before treatment v At 7 months follow-up
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.011
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	before treatment vs at 10 months FU
Comparison groups	Before treatment v At 10 months follow-up
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.066
Method	Wilcoxon (Mann-Whitney)

Secondary: Change in expression of neurotrophins (NT3) in CSF (cerebrospinal fluid) samples

End point title	Change in expression of neurotrophins (NT3) in CSF (cerebrospinal fluid) samples
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End point description:

Changes in expression of neurotrophins in CSF (CerebroSpinal Fluid) samples obtained previously to first administration of cell therapy, and previously to the last administration, at month 10, in order to study the variability in the expression of neurotrophins along time. The mean+SD (standard deviation) at each time point was obtained. The tested neurotrophin was: NT3 (neurotrophin-3).

End point type	Secondary
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End point timeframe:

Basal, 4, 7 and 10 months after the administration

End point values	Before treatment	At 4 months follow-up	At 7 months follow-up	At 10 months follow-up
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	10	8 ^[8]	10
Units: pg/ml				
arithmetic mean (standard deviation)	175.00 (± 53.39)	205.66 (± 35.20)	213.04 (± 77.44)	188.00 (± 50.59)

Notes:

[8] - This data was not obtained in two patients.

Statistical analyses

Statistical analysis title	before treatment vs at 4 months FU
Comparison groups	Before treatment v At 4 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.114
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	before treatment vs at 7 months FU
Comparison groups	Before treatment v At 7 months follow-up
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.401
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	before treatment vs at 10 months FU
Comparison groups	Before treatment v At 10 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.508
Method	Wilcoxon (Mann-Whitney)

Secondary: Change in expression of neurotrophins (NT4) in CSF (cerebrospinal fluid) samples

End point title	Change in expression of neurotrophins (NT4) in CSF (cerebrospinal fluid) samples
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End point description:

Changes in expression of neurotrophins in CSF (CerebroSpinal Fluid) samples obtained previously to first administration of cell therapy, and previously to the last administration, at month 10, in order to study the variability in the expression of neurotrophins along time. The mean+SD (standard deviation) at each time point was obtained. The tested neurotrophin was: NT4 (neurotrophin-4).

End point type	Secondary
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End point timeframe:

Basal, 4, 7 and 10 months after the administration

End point values	Before treatment	At 4 months follow-up	At 7 months follow-up	At 10 months follow-up
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	10	8 ^[9]	10
Units: pg/ml				
arithmetic mean (standard deviation)	3.72 (± 0.87)	3.40 (± 0.57)	3.85 (± 0.73)	4.07 (± 1.50)

Notes:

[9] - This data was not obtained in two patients.

Statistical analyses

Statistical analysis title	before treatment vs at 4 months FU
Comparison groups	Before treatment v At 4 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.445
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	before treatment vs at 7 months FU
Comparison groups	Before treatment v At 7 months follow-up
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.889
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	before treatment vs at 10 months FU
Comparison groups	Before treatment v At 10 months follow-up
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.441
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

During the entire clinical trial (Up to 12 months)

Adverse event reporting additional description:

Adverse events were collected asking questions to the participants and performing general clinical examinations and neurological examinations.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.1
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Reporting groups

Reporting group title	Arm 1
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Reporting group description:

Treatment arm

Serious adverse events	Arm 1		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 10 (10.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Arm 1		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 10 (90.00%)		
Injury, poisoning and procedural complications			
Wound			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Vascular disorders			

Hypertension subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Syncope subjects affected / exposed occurrences (all) Pain in coccyx subjects affected / exposed occurrences (all)	3 / 10 (30.00%) 4 1 / 10 (10.00%) 1 1 / 10 (10.00%) 1		
General disorders and administration site conditions Local pain subjects affected / exposed occurrences (all) Hyperthermia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1 1 / 10 (10.00%) 1		
Renal and urinary disorders Urinary retention subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Musculoskeletal and connective tissue disorders Leg pain subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) Neck pain subjects affected / exposed occurrences (all) Back pain	1 / 10 (10.00%) 1 1 / 10 (10.00%) 1 1 / 10 (10.00%) 1		

subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Infected skin ulcer			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 November 2015	Incorporation of the Geffner and NBD scales as efficacy variables. Addition of non-harmful events classification.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The main limitation of the study is the small number of subjects analysed

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/28089079>