Clinical trial results:
Evaluate the efficacy of the cell therapy with NC1 medication in patients with post-traumatic syringomyelia

Summary

EudraCT number	2015-002383-16
Trial protocol	ES
Global end of trial date	07 February 2018

Results information

Result version number	v1 (current)
This version publication date	03 April 2022
First version publication date	03 April 2022

Trial information

Trial identification

Sponsor protocol code	CME-LEM4

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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,
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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 February 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 February 2018
Global end of trial reached?	Yes
Global end of trial date	07 February 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To analyze the potential clinical efficacy of the administration in the intrathecal compartment, (intramedullary and in the subarachnoid space), of the medication NC1, to improve the neurological sequels of patients with established chronic spinal cord injury (LEM) and post-traumatic syringomyelia.

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:

From the start of treatment until the end of the trial (month 6 after CME administration) patients performed physical therapy exercises.

Evidence for comparator: -

Actual start date of recruitment	07 March 2016
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
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: 6
Worldwide total number of subjects	6
EEA total number of subjects	6

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)	6

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The planned duration of the clinical trial was 12 months. The duration of the recruitment phase was 6 months, and the duration of the follow-up period after treatment was 6 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	6
Number of subjects completed	6

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

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 syrinx of a single dose of 300 x 10^6 autologous expanded mesenchymal stromal cells, supported in autologous plasma, through a surgical approach to the spinal cord.

Number of subjects in period 1	Arm 1
Started	6
Completed	6

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	6	6	
Age categorical			
Age ranged between 30 and 50 years (mean ± standard deviation [SD], 39 ± 7.6 years)			
Units: Subjects			
Adults (18-64 years)	6	6	
Gender categorical Units: Subjects			
Female	0	0	
Male	6	6	
American Spinal Injury Association Impairment Scale (ASIA) grade Units: Subjects			
ASIA A	3	3	
ASIA B	2	2	
ASIA D	1	1	
Spinal cord injury (SCI) vertebral level Units: Subjects			
D3	1	1	
D4	1	1	
D5	2	2	
D8	1	1	
L1	1	1	
Time since Spinal cord injury (SCI) Units: Subjects			
5,75 years	1	1	
6,16 years	1	1	
8,07 years	1	1	
17,01 years	1	1	
17,72 years	1	1	
27,68 years	1	1	

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	

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.	
End point type	Primary
End point timeframe: Between the subject´s inclusion in the study and the end of the follow-up (FU) period.	

End point values	Before treatment	At 3 months follow-up	At 6 months follow-up	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	6	6	6	
Units: Score				
arithmetic mean (standard deviation)				
Total Score	143.00 (± 16.20)	144.3 (± 16.69)	149.00 (± 17.18)	
Pin Prick Score	41.67 (± 5.27)	43.17 (± 6.36)	44.67 (± 7.03)	
Light Touch Score	50.33 (± 11.76)	50.17 (± 11.55)	53.33 (± 11.94)	

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	12
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.37
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	12
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.12
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	12
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.25
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	12
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.06
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	12
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	> 0.99
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	12
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.25
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:

IANR-SCIFRS scale: the SCI Functional Rating Scale of the International Association of Neurorestoratology scale. This scale evaluates the global spinal cord function.
Efficacy was assessed by taking into account the variation in the scores on the different scales between the subject´s inclusion in the study and the scores obtained at the end of the follow-up period.

End point type	Primary

End point timeframe:

Between the subject´s inclusion in the study and the end of the follow-up period.

End point values	Before treatment	At 3 months follow-up	At 6 months follow-up	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	6	6	6	
Units: score				
arithmetic mean (standard deviation)	29.33 (± 7.86)	32.33 (± 6.31)	34.83 (± 3.86)	

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	12
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.06
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	12
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.06
Method	Wilcoxon (Mann-Whitney)

Primary: Change in the score in VAS scale

End point title	Change in the score in VAS scale

End point description:

VAS: Visual Analog Scale. This scale evaluates neuropathic pain.
Efficacy was assessed by taking into account the variation in the scores on the different scales between the subject´s inclusion in the study and the scores obtained at the end of the follow-up period.

End point type	Primary

End point timeframe:

Between the subject´s inclusion in the study and the end of the follow-up period.

End point values	Before treatment	At 3 months follow-up	At 6 months follow-up	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	6	6	6	
Units: score				
arithmetic mean (standard deviation)	2.00 (± 3.16)	1.33 (± 2.42)	1.00 (± 2.44)	

Statistical analyses

Statistical analysis title	Before treatment vs at 3 months FU
Comparison groups	At 3 months follow-up v Before treatment
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.25
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	12
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.25
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. Efficacy was assessed by taking into account the variation in the scores on the different scales between the subject´s inclusion in the study and the scores obtained at the end of the follow-up period.	
End point type	Primary
End point timeframe:	
Between the subject´s inclusion in the study and the end of the follow-up period.	

End point values	Before treatment	At 3 months follow-up	At 6 months follow-up	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	6	6	6	
Units: score				
arithmetic mean (standard deviation)	1.66 (± 1.21)	1.33 (± 1.03)	1.16 (± 0.75)	

Statistical analyses

Statistical analysis title	Before treatment vs at 3 months FU
Comparison groups	At 3 months follow-up v Before treatment
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	> 0.99
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	12
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.5
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 the scores on the different scales between the subject´s inclusion in the study and the scores obtained at the end of the follow-up period.	
End point type	Primary
End point timeframe:	
Between the subject´s inclusion in the study and the end of the follow-up period.	

End point values	Before treatment	At 3 months follow-up	At 6 months follow-up	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	6	6	6	
Units: score				
arithmetic mean (standard deviation)	1.75 (± 1.17)	1.58 (± 1.35)	1.50 (± 0.83)	

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	12
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	> 0.99
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	12
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.5
Method	Wilcoxon (Mann-Whitney)

Primary: Change in the score in Geffner scale	
End point title	Change in the score in Geffner scale
End point description:	
Geffner scale was used for the study of bladder function. Efficacy was assessed by taking into account the variation in the scores on the different scales between the subject´s inclusion in the study and the scores obtained at the end of the follow-up period.	
End point type	Primary
End point timeframe:	
Between the subject´s inclusion in the study and the end of the follow-up period.	

End point values	Before treatment	At 3 months follow-up	At 6 months follow-up	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	6	6	6	
Units: score				
arithmetic mean (standard deviation)	1.83 (± 1.47)	2.50 (± 1.22)	2.83 (± 1.47)	

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	12
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.5
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	12
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.25
Method	Wilcoxon (Mann-Whitney)

Primary: Change in the score in NBD scale

End point title	Change in the 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 the scores on the different scales between the subject´s inclusion in the study and the scores obtained at the end of the follow-up period.

End point type	Primary

End point timeframe:

Between the subject´s inclusion in the study and the end of the follow-up period.

End point values	Before treatment	At 3 months follow-up	At 6 months follow-up	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	6	6	6	
Units: score				
arithmetic mean (standard deviation)	14.67 (± 6.91)	9.83 (± 3.92)	8.50 (± 5.54)	

Statistical analyses

Statistical analysis title	Before treatment vs at 3 months FU
Comparison groups	At 3 months follow-up v Before treatment
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.12
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Before treatment vs at 6 months FU
Comparison groups	At 6 months follow-up v Before treatment
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.12
Method	Wilcoxon (Mann-Whitney)

Primary: Change in parameters of ano-rectal manometry: pressure of rectal sphincter at rest

End point title	Change in parameters of ano-rectal manometry: pressure of rectal sphincter at rest[1]

End point description:

Functional ano-rectal studies were performed using a High Resolution Manometry equipment (Solar GI HRM, MMS B.V., Enschede, NL) and a water perfused 8 channel catheter with a balloon at the tip. With the patient in a left lateral position, with hips and knees bent, and after a rest period of 5 to 10 minutes, the parameters were assessed.
Descriptive analysis was performed for anorectal manomety parameters. Two subjects (2 and 5) showed improvement achieving a higher mean pressure of rectal sphincter.

End point type	Primary

End point timeframe:

Between the subject´s inclusion in the study and the end of the follow-up period.

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: Descriptive analysis was performed for anorectal manomety parameters, comparing the results with the baseline values.

End point values	Before treatment	At 6 months follow-up		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	6		
Units: mmHG				
number (not applicable)				
Subject 1	50	53		
Subject 2	25	83		
Subject 3	31	37		
Subject 4	69	36		
Subject 5	60	79		
Subject 6	68	54		

Statistical analyses

No statistical analyses for this end point

Primary: Change in parameters of ano-rectal manometry: pressure of anal contraction

End point title	Change in parameters of ano-rectal manometry: pressure of anal contraction[2]

End point description:

Functional ano-rectal studies were performed using a High Resolution Manometry equipment (Solar GI HRM, MMS B.V., Enschede, NL) and a water perfused 8 channel catheter with a balloon at the tip. With the patient in a left lateral position, with hips and knees bent, and after a rest period of 5 to 10 minutes, the parameters were assessed.
Descriptive analysis was performed for anorectal manomety parameters. Three patients (1, 3 and 5) showed improvement achieving a higher anal contraction pressure.
00 = non computable

End point type	Primary

End point timeframe:

Between the subject´s inclusion in the study and the end of the follow-up period.

Notes:

[2] - 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: Descriptive analysis was performed for anorectal manomety parameters, comparing the results with the baseline values.

End point values	Before treatment	At 6 months follow-up		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	6		
Units: mmHg				
number (not applicable)				
Subject 1	50	70		
Subject 2	35	00		
Subject 3	40	61		
Subject 4	82	36		
Subject 5	71	164		
Subject 6	102	60		

Statistical analyses

No statistical analyses for this end point

Primary: Change in parameters of ano-rectal manometry: first sensation of rectal filling

End point title	Change in parameters of ano-rectal manometry: first sensation of rectal filling[3]

End point description:

Functional ano-rectal studies were performed using a High Resolution Manometry equipment (Solar GI HRM, MMS B.V., Enschede, NL) and a water perfused 8 channel catheter with a balloon at the tip. With the patient in a left lateral position, with hips and knees bent, and after a rest period of 5 to 10 minutes, the parameters were assessed.
Descriptive analysis was performed for anorectal manometry parameters. Three patients (2, 3 and 5) showed improvement of first rectal filling sensation.
00 = absent

End point type	Primary

End point timeframe:

Between the subject´s inclusion in the study and the end of the follow-up period.

Notes:

[3] - 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: Descriptive analysis was performed for anorectal manometry parameters, comparing the results with the baseline values.

End point values	Before treatment	At 6 months follow-up		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	6		
Units: mmHg				
number (not applicable)				
Subject 1	00	00		
Subject 2	00	180		
Subject 3	150	80		
Subject 4	100	00		
Subject 5	00	60		
Subject 6	00	00		

Statistical analyses

No statistical analyses for this end point

Primary: Change in urodynamic studies: first sensation at filling

End point title	Change in urodynamic studies: first sensation at filling[4]

End point description:

Urodynamic studies were performed using using a Solar Luna equipment (Medical Measurement

Systems Inc., Dover, NH, USA). At the end of the study, all of the patients showed improvement in two or more of the parameters studied.
Four patients (1, 3, 4 and 6) improved in first sensation at filling.

End point type	Primary

End point timeframe:

Between the subject´s inclusion in the study and the end of the follow-up period.

Notes:

[4] - 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: Descriptive analysis was performed for urodinamic studies, comparing the results with the baseline values.

End point values	Before treatment	At 6 months follow-up		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	6		
Units: cc				
number (not applicable)				
Subject 1	454	360		
Subject 2	560	610		
Subject 3	307	292		
Subject 4	38	33		
Subject 5	140	212		
Subject 6	166	134		

Statistical analyses

No statistical analyses for this end point

Primary: Change in urodynamic studies: bladder capacity at filling

End point title	Change in urodynamic studies: bladder capacity at filling[5]

End point description:

Urodynamic studies were performed using using a Solar Luna equipment (Medical Measurement Systems Inc., Dover, NH, USA). At the end of the study, all of the patients showed improvement in two or more of the parameters studied.
Four patients (2, 4, 5 and 6) improved in maximum cystometric capacity.

End point type	Primary

End point timeframe:

Between the subject´s inclusion in the study and the end of the follow-up period.

Notes:

[5] - 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: Descriptive analysis was performed for urodinamic studies, comparing the results with the baseline values.

End point values	Before treatment	At 6 months follow-up		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	6		
Units: cc				
number (not applicable)				
Subject 1	456	412		
Subject 2	573	611		

Subject 3	346	324		
Subject 4	171	209		
Subject 5	147	221		
Subject 6	169	431		

Statistical analyses

No statistical analyses for this end point

Primary: Change in urodynamic studies: detrusor pressure at filling

End point title	Change in urodynamic studies: detrusor pressure at filling[6]

End point description:

Urodynamic studies were performed using using a Solar Luna equipment (Medical Measurement Systems Inc., Dover, NH, USA). At the end of the study, all of the patients showed improvement in two or more of the parameters studied.
Three patients (2, 3 and 5) showed decrease in detrusor pressure at filling.

End point type	Primary

End point timeframe:

Between the subject´s inclusion in the study and the end of the follow-up period.

Notes:

[6] - 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: Descriptive analysis was performed for urodinamic studies, comparing the results with the baseline values.

End point values	Before treatment	At 6 months follow-up		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	6		
Units: cm H2O				
number (not applicable)				
Subject 1	30	51		
Subject 2	19	10		
Subject 3	4	3		
Subject 4	10	111		
Subject 5	81	61		
Subject 6	8	33		

Statistical analyses

No statistical analyses for this end point

Primary: Change in urodynamic studies: bladder compliance at filling

End point title	Change in urodynamic studies: bladder compliance at filling[7]

End point description:

Urodynamic studies were performed using using a Solar Luna equipment (Medical Measurement Systems Inc., Dover, NH, USA). At the end of the study, all of the patients showed improvement in two or more of the parameters studied.
Three patients (2, 3 and 5) improved in bladder compliance at filling.

End point type	Primary

End point timeframe:

Between the subject´s inclusion in the study and the end of the follow-up period.

Notes:

[7] - 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: Descriptive analysis was performed for urodinamic studies, comparing the results with the baseline values.

End point values	Before treatment	At 6 months follow-up		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	6		
Units: cc				
number (not applicable)				
Subject 1	15	8		
Subject 2	30	61		
Subject 3	86	108		
Subject 4	17	2		
Subject 5	2	4		
Subject 6	21	13		

Statistical analyses

No statistical analyses for this end point

Primary: Change in urodynamic studies: postmictional residue

End point title	Change in urodynamic studies: postmictional residue[8]

End point description:

Urodynamic studies were performed using using a Solar Luna equipment (Medical Measurement Systems Inc., Dover, NH, USA). At the end of the study, all of the patients showed improvement in two or more of the parameters studied.
Four patients (1, 3, 4 and 5) improved in postmictional residue.

End point type	Primary

End point timeframe:

Between the subject´s inclusion in the study and the end of the follow-up period.

Notes:

[8] - 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: Descriptive analysis was performed for urodinamic studies, comparing the results with the baseline values.

End point values	Before treatment	At 6 months follow-up		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	6		
Units: cc				
number (not applicable)				
Subject 1	268	106		
Subject 2	573	611		
Subject 3	346	324		
Subject 4	171	87		

Subject 5	127	50		
Subject 6	75	431		

Statistical analyses

No statistical analyses for this end point

Primary: Change in spinal cord morphology, after neuroimaging study: length of syrinx

End point title	Change in spinal cord morphology, after neuroimaging study: length of syrinx

End point description:

Before treatment, in magnetic resonance, all of the patients had a large syringomyelic cavity on either side of the SCI area. The extension of the syrinx ranged between 87 and 300 mm (mean ± SD, 210.3 ± 90.94 mm).
The measurements were taken by means of software associated with MR- 3T equipment (Philips Intera Achieva XR, v 263.9; Philips Healthcare) on sagittal T2-weighted images and MR-myelography images achieved with sequences of "turbo spin-echo"
The measurements must be considered as approximate due to the difficulty of obtaining strictly superimposable images in sequential studies.

End point type	Primary

End point timeframe:

Between the subject´s inclusion in the study and the end of the follow-up period.

End point values	Before treatment	At 6 months follow-up		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	6		
Units: mm				
number (not applicable)				
Subject 1	120	113		
Subject 2	87	47		
Subject 3	280	280		
Subject 4	195	195		
Subject 5	300	142		
Subject 6	280	100		

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	12
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.12
Method	Wilcoxon (Mann-Whitney)

Primary: Change in spinal cord morphology, after neuroimaging study: width of syrinx

End point title	Change in spinal cord morphology, after neuroimaging study: width of syrinx

End point description:

Before treatment, in magnetic resonance, all of the patients had a large syringomyelic cavity on either side of the SCI area. In the medium sagittal plain, the width of the syrinx ranged between 10 and 20 mm (mean ± SD, 12.05 ± 3.97 mm).
The measurements were taken by means of software associated with MR- 3T equipment (Philips Intera Achieva XR, v 263.9; Philips Healthcare) on sagittal T2-weighted images and MR-myelography images achieved with sequences of "turbo spin-echo"
The measurements must be considered as approximate due to the difficulty of obtaining strictly superimposable images in sequential studies.

End point type	Primary

End point timeframe:

Between the subject´s inclusion in the study and the end of the follow-up period.

End point values	Before treatment	At 6 months follow-up		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	6		
Units: mm				
number (not applicable)				
Subject 1	10.3	6.3		
Subject 2	10.0	1.2		
Subject 3	10.0	8.0		
Subject 4	10.0	4.6		
Subject 5	20.0	14.2		
Subject 6	12.0	4.0		

Statistical analyses

Statistical analysis title	Before treatment vs at 6 months FU
Comparison groups	At 6 months follow-up v Before treatment
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.03
Method	Wilcoxon (Mann-Whitney)

Primary: Change in spinal cord morphology, after neuroimaging study: syrinx/canal index

End point title	Change in spinal cord morphology, after neuroimaging study: syrinx/canal index

End point description:

The syrinx/canal index was studied as an index that indirectly values intramedullary tension.

End point type	Primary

End point timeframe:

Between the subject´s inclusion in the study and the end of the follow-up period.

End point values	Before treatment	At 6 months follow-up		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	6		
Units: S/C Index				
arithmetic mean (standard deviation)	0.84 (± 0.24)	0.33 (± 0.19)		

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	12
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.03
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)[9]

End point description:

End point type	Primary

End point timeframe:

Between the subject´s inclusion in the study and the end of the follow-up period.

Notes:

[9] - 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 with the baseline values.

End point values	Arm 1			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Subjects				
Improvement in SSEP	2			
No improvement in SSEP	4			

Statistical analyses

No statistical analyses for this end point

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

End point title	Change in neurophysiological parameters: improvement in Motor Evoked Potentials (MEP)[10]

End point description:

End point type	Primary

End point timeframe:

Between the subject´s inclusion in the study and the end of the follow-up period.

Notes:

[10] - 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 with the baseline values.

End point values	Arm 1			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Subjects				
Improvement in MEP	1			
No improvement in MEP	5			

Statistical analyses

No statistical analyses for this end point

Primary: Change in neurophysiological parameters: improvement in sensitivity conduction

End point title	Change in neurophysiological parameters: improvement in sensitivity conduction[11]

End point description:

End point type	Primary

End point timeframe:

Between the subject´s inclusion in the study and the end of the follow-up period.

Notes:

[11] - 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 with the baseline values.

End point values	Arm 1			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Subjects				
Improvement	2			
No improvement	4			

Statistical analyses

No statistical analyses for this end point

Primary: Change in neurophysiological parameters: improvement in motor conduction

End point title	Change in neurophysiological parameters: improvement in motor conduction[12]

End point description:

End point type	Primary

End point timeframe:

Between the subject´s inclusion in the study and the end of the follow-up period.

Notes:

[12] - 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 with the baseline values.

End point values	Arm 1			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Subjects				
Improvement	1			
No improvement	5			

Statistical analyses

No statistical analyses for this end point

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

End point title	Change in neurophysiological parameters: improvement in voluntary muscle contraction[13]

End point description:

End point type	Primary

End point timeframe:

Between the subject´s inclusion in the study and the end of the follow-up period.

Notes:

[13] - 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 with the baseline values.

End point values	Arm 1			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Subjects				
Improvement	1			
No improvement	5			

Statistical analyses

No statistical analyses for this end point

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

End point title	Change in neurophysiological parameters: presence of infralesional activity muscle reinnervation[14]

End point description:

End point type	Primary

End point timeframe:

Between the subject´s inclusion in the study and the end of the follow-up period.

Notes:

[14] - 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 with the baseline values.

End point values	Arm 1			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Subjects				
Improvement	2			
No improvement	4			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
During the entire clinical trial	
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

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups	
Reporting group title	Arm 1
Reporting group description:	
Treatment arm	

Serious adverse events	Arm 1		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 6 (16.67%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 6 (16.67%)		
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	3 / 6 (50.00%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
General disorders and administration site conditions			

Temperature regulation disorder subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Skin and subcutaneous tissue disorders Thermal burn subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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.

New studies with a greater number of cases are required.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/29784434