EU Clinical Trials Register

Clinical trial results:

Treatment of degenerative disc disease with allogenic mesenchymal cells—MSV (Mesenchymal stromal cells (MSCs) extracted from the bone marrow and expanded "in vivo" following the GMP procedures developed by the institute of biology and molecular genetics from Valladolid).

Summary

EudraCT number	2012-004444-30
Trial protocol	ES
Global end of trial date	15 December 2015

Results information

Result version number	v1 (current)
This version publication date	20 June 2021
First version publication date	20 June 2021
Summary attachment (see zip file)	Intervertebral disc repair by allogeneic mesenchymal bone marrow cells: a randomized controlled trial (Publicación-Noriega 2017.pdf)
	Supplementary data (Noriega-2017-Intervertebral Disc Repair by Allogeneic_SUPPLEMENTAL DIGITAL CONTENT.pdf)

Trial information

Trial identification

Sponsor protocol code	Disc_allo_MSV

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01860417
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CITOSPIN
Sponsor organisation address	Paseo de Belén, 11 Campus Miguel Delibes, Valladolid, Spain,
Public contact	Dr. Javier García-Sancho, CITOSPIN , 34 983184827, jgsancho@uva.es
Scientific contact	Dr. Javier García-Sancho, CITOSPIN , 34 983184827, jgsancho@uva.es

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	24 April 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 December 2015
Global end of trial reached?	Yes
Global end of trial date	15 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Feasibility and security of allogeneic bone marrow (MSCs) cells local use for degenerative disc disease treatment.

Protection of trial subjects:

A continuous follow-up of adverse events was conducted through the study to detect and solve any discomfort or untoward medical occurrence that the patients may experience.
Besides the experimental treatment (MSC cells or control with 1% mepivacaine) the patients will receive the usual treatment based on rehabilitative physiotherapy, postural hygiene and pharmacotherapy.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	26 November 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 24
Worldwide total number of subjects	24
EEA total number of subjects	24

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)	24

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment was performed between July 2013 and March 2014. The study was conducted in only one center "Hospital Clínico Universitario de Valladolid - Spain"

Pre-assignment

Screening details:

Screening was done among patients with degenerative disease of 1 or 2 lumbar discs with predominant back pain after conservative treatment (physical and medical) for over 6 months. 26 patients were screened (1 decided no participate and 1 was excluded because received an incorrect number of cells). 24 subjects participated,

Period 1

Period 1 title	Treatment
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind[1]
Roles blinded	Subject, Data analyst

Blinding implementation details:

While the investigator knew which treatment was administered to the patient, neither the patient nor the data analyst knew it. Procedures for both arms were the same, The test group received allogeneic bone marrow MSCs by intradiscal injection under local anesthesia and the control group received a sham infiltration of paravertebral musculature with the anesthetic. The nature of the treatments were code-protected so the blind is preserved to the analysist

Arms

Are arms mutually exclusive?	Yes
Arm title	Experimental

Arm description:

12 patients were randomly allocated to this arm and received allogeneic bone marrow MSCs by intradiscal injection of 25×10e6 cells per segment under local anesthesia.

Arm type	Experimental
Investigational medicinal product name	Allogenic bone marrow mesenquimal cells (MSCs)
Investigational medicinal product code	
Other name	MSV
Pharmaceutical forms	Injection
Routes of administration	Intradiscal use

Dosage and administration details:

The product was administered in one intervention by intradiscal injection of 25×10e6 cells in 2 ml of saline suplemened with human albumin (0,5%) and glucose (5mM) per disc, under local anesthesia. Bone marrow was obtained from 5 healthy donors and processed using GMP conditions in the IBGM Cell Production Unit. Isolations were carried out with the following parameters (mean ± SD; n = 5, 4 males and 1 woman): bone marrow volume = 10e5 ± 5 ml, average number of mononuclear cells obtained = 1.23 ± 0.25×10e9, expansion time = 27 ± 2 days, number of MSC injected into each disc = 25 ×10e6, suspended in Ringer-lactate at 12.5×1e06 cells/ml, and viability >98±1%. A serum sample from each donor was obtained to screen for human immunodeficiency, hepatitis B, and hepatitis C virus by Nucleic Acid Amplification Technology. The cells obtained from each donor were used for 1-3 recipients. Immune matching was not attempted.

Arm title	Active Control

Arm description:

12 patients were randomly assigned to the control group. All procedures were the same than the Experimental arm. The control group received a sham infiltration of paravertebral musculature with the anesthetic: saline containing 1% mepivacaine (1 ml of 2% mepivacaine + 1 ml of saline).

Arm type	Active comparator

Investigational medicinal product name	Mepivacaine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intradiscal use

Dosage and administration details:

The patients included in the control group received the treatment, mepivacain without MSC cells, in one intervention. They received a sham infiltration of paravertebral musculature with the anesthetic, 1% mepivacaine in each affected disc. The techniques and procedures were identical than the experimental arm.

Notes:

[1] - The roles blinded appear to be inconsistent with a double blind trial.

Justification: The study has been categorized as double blind as only the investigators, that perfomed the intervention knew the treatment assigned to the patient. The patients, radiologists, care providers, and persons assessing the outcomes of the assay were blinded after assignment.

Number of subjects in period 1	Experimental	Active Control
Started	12	12
Completed	12	12

Period 2

Period 2 title	Follow Up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind[2]
Roles blinded	Subject, Data analyst

Blinding implementation details:

While the investigator knew which treatment was administered to the patient, neither the patient nor the data analyst knew it. Procedures for both arms were the same, The test group received allogeneic bone marrow MSCs by intradiscal injection under local anesthesia and the control group received a sham infiltration of paravertebral musculature with the anesthetic. The nature of the treatments were codeprotected
so the blind is preserved to the analysist

Arms

Are arms mutually exclusive?	Yes
Arm title	Experimental

Arm description:

12 patients were randomly allocated to this arm and received allogeneic bone marrow MSCs by intradiscal injection of 25×10e6 cells per segment under local anesthesia.

Arm type	Experimental
Investigational medicinal product name	Allogenic bone marrow mesenquimal cells (MSCs)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intradiscal use

Dosage and administration details:

The product was administered in one intervention by intradiscal injection of 25×10e6 cells in 2 ml of

saline suplemened with human albumin (0,5%) and glucose (5mM) per disc, under local anesthesia. Bone marrow was obtained from 5 healthy donors and processed using GMP conditions in the IBGM Cell Production Unit. Isolations were carried out with the following parameters (mean ± SD; n = 5, 4 males and 1 woman): bone marrow volume = 10e5 ± 5 ml, average number of mononuclear cells obtained = 1.23 ± 0.25×10e9, expansion time = 27 ± 2 days, number of MSC injected into each disc = 25 ×10e6, suspended in Ringer-lactate at 12.5×1e06 cells/ml, and viability >98±1%. A serum sample from each donor was obtained to screen for human immunodeficiency, hepatitis B, and hepatitis C virus by Nucleic Acid Amplification Technology. The cells obtained from each donor were used for 1-3 recipients. Immune matching was not attempted.

Arm title	Active Control

Arm description:

12 patients were randomly assigned to the control group. All the procedures were the same than the Experimental arm. The control group received a sham infiltration of paravertebral musculature with the anesthetic.

Arm type	Active comparator
Investigational medicinal product name	Mepivacaine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intradiscal use

Dosage and administration details:

The patients included in the Control group received the treatment (Mepivacaine without MSC cells) in one intervention. They received a sham infiltration of paravertebral musculature with the anesthetic, 1% mepivacain in each affected disc. The techniques and procedures were identicaln than the experimental arm.

Notes:

[2] - The roles blinded appear to be inconsistent with a double blind trial.

Justification: The study has been categorized as double blind as only the investigators, that perfomed the intervention knew the treatment assigned to the patient. The patients, radiologists, care providers, and persons assessing the outcomes of the assay were blinded after assignment.

Number of subjects in period 2	Experimental	Active Control
Started	12	12
Completed	12	12

Baseline characteristics

Reporting groups

Reporting group title	Treatment

Reporting group description:

A subject will be included in the analysis if he/she has been treated with MSC or active control as described in the protocol.

Reporting group values	Treatment	Total	
Number of subjects	24	24	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Units: years			
arithmetic mean	38		
standard deviation	± 8.59	-	
Gender categorical			
Units: Subjects			
Female	7	7	
Male	17	17	

Subject analysis sets

Subject analysis set title	Efficacy
Subject analysis set type	Per protocol

Subject analysis set description:

This analysis included all the subjects that have been treated (either control or active cells), with no major protocol deviations and that had, at least, data from one efficacy assessment.

Subject analysis set title	Safety
Subject analysis set type	Full analysis

Subject analysis set description:

This set included all patients that have received the intervention (either control or allogeneic mesenchymal bone marrow cells)

Reporting group values	Efficacy	Safety	
Number of subjects	24	24	
Age categorical			
Units: Subjects			
In utero			

Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
arithmetic mean	38	38	
standard deviation	± 8.59	± 8.59	
Gender categorical Units: Subjects			
Female	7	7	
Male	17	17	

End points

End points reporting groups

Reporting group title	Experimental
Reporting group description:	
12 patients were randomly allocated to this arm and received allogeneic bone marrow MSCs by intradiscal injection of 25×10e6 cells per segment under local anesthesia.	
Reporting group title	Active Control
Reporting group description:	
12 patients were randomly assigned to the control group. All procedures were the same than the Experimental arm. The control group received a sham infiltration of paravertebral musculature with the anesthetic: saline containing 1% mepivacaine (1 ml of 2% mepivacaine + 1 ml of saline).	
Reporting group title	Experimental
Reporting group description:	
12 patients were randomly allocated to this arm and received allogeneic bone marrow MSCs by intradiscal injection of 25×10e6 cells per segment under local anesthesia.	
Reporting group title	Active Control
Reporting group description:	
12 patients were randomly assigned to the control group. All the procedures were the same than the Experimental arm. The control group received a sham infiltration of paravertebral musculature with the anesthetic.	
Subject analysis set title	Efficacy
Subject analysis set type	Per protocol
Subject analysis set description:	
This analysis included all the subjects that have been treated (either control or active cells), with no major protocol deviations and that had, at least, data from one efficacy assessment.	
Subject analysis set title	Safety
Subject analysis set type	Full analysis
Subject analysis set description:	
This set included all patients that have received the intervention (either control or allogeneic mesenchymal bone marrow cells)	

Primary: Safety

End point title	Safety[1]
End point description:	
The number of participants with adverse events was used as a measure of safety and tolerability.	
End point type	Primary
End point timeframe:	
Adverse events reporting started when after the administration of the study treatments, and lasted up to the last visit of each patient at the end of the follow-up period, 12 months after the intervention.	

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: The primary objective of the study was to test the safety and tolerability of the intervention. Number of participants with adverse events was be used as a measure of safety and tolerability, but no further statisctical analysis was planned in the protocol at this stage of the development, for this primary outcome.

End point values	Experimental	Active Control	Safety	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	12	12	24	
Units: Number of AEs per arm	5	9	14	

Statistical analyses

No statistical analyses for this end point

Secondary: Pain and disability evolution

End point title	Pain and disability evolution

End point description:

Improvement in the composite variable which includes pain and disability, 1 year after intervention was plotted as a function of the initial pain score or disability index. Results for the relief of lumbar pain and Oswestry disability index were all included for both, control and cell-treated patients.

End point type	Secondary

End point timeframe:

Improvement since the baseline (before intervention) up to the end of the follow-up period, 12 months after the intervention

End point values	Experimental	Active Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: unit(s)				
arithmetic mean (standard error)	0.28 (± 0.07)	0.15 (± 0.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Evolution of affected disc(s) by quantitative MRI Ratio 12/6months

End point title	Evolution of affected disc(s) by quantitative MRI Ratio 12/6months

End point description:

Ratio discs density betwewn 12 and 6 months after transplantation. To homogenize the results of different patients, the water content values of the affected discs were normalized to the values obtained from the healthy discs in the same individual; for these purposes, the density of the affected segments was divided by the average value of the healthy discs. Finally, the value after the treatment was divided by the baseline value.

End point type	Secondary

End point timeframe:

From the baseline, prior the intervention, to the end of the follow-up, 12 months after the intervention

End point values	Experimental	Active Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: percent				
arithmetic mean (standard error)	22 (± 11)	6 (± 8)		

Statistical analyses

No statistical analyses for this end point

Secondary: SF-12 Physical Component 3 months

End point title	SF-12 Physical Component 3 months
End point description:	
Short form-12 (SF-12) of the physical component of the life quality questionnaire, measured 3 months after the intervention.	
End point type	Secondary
End point timeframe:	
3 months after the intervention	

End point values	Experimental	Active Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: unit(s)				
arithmetic mean (standard error)	47 (± 3)	43 (± 3)		

Statistical analyses

No statistical analyses for this end point

Secondary: SF-12 Physical Component 6 months

End point title	SF-12 Physical Component 6 months
End point description:	
Physical component of the short form-12 (SF-12) life quality questionnaire measured 6 months after the intervention.	
End point type	Secondary
End point timeframe:	
6 months after the intervention	

End point values	Experimental	Active Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: units				
arithmetic mean (standard error)	46 (± 3)	39 (± 3)		

Statistical analyses

No statistical analyses for this end point

Secondary: SF-12 Physical Component 12 months

End point title	SF-12 Physical Component 12 months
End point description:	
Physical component of the short form-12 (SF-12) life quality questionnaire measured 12 months after the intervention.	
End point type	Secondary
End point timeframe:	
12 months after the intervention	

End point values	Experimental	Active Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: units				
arithmetic mean (standard error)	45 (± 3)	42 (± 3)		

Statistical analyses

No statistical analyses for this end point

Secondary: SF-12 Mental Component 3 months

End point title	SF-12 Mental Component 3 months
End point description:	
Mental component of the short form-12 (SF-12) life quality questionnaire measured 3 months after the intervention.	
End point type	Secondary
End point timeframe:	
3 months after the intervention	

End point values	Experimental	Active Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: units				
arithmetic mean (standard error)	50 (± 2)	46 (± 3)		

Statistical analyses

No statistical analyses for this end point

Secondary: SF-12 Mental Component 6 months

End point title	SF-12 Mental Component 6 months
End point description:	
Mental component of the short form-12 (SF-12) life quality questionnaire measured 6 months after the intervention.	
End point type	Secondary
End point timeframe:	
6 months after intervention	

End point values	Experimental	Active Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: units				
arithmetic mean (standard error)	52 (± 2)	48 (± 3)		

Statistical analyses

No statistical analyses for this end point

Secondary: SF-12 Mental Component 12 months

End point title	SF-12 Mental Component 12 months
End point description:	
Mental component of the short form-12 (SF-12) life quality questionnaire measured 12 months after the intervention.	
End point type	Secondary
End point timeframe:	
12 months after intervention	

End point values	Experimental	Active Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: units				
arithmetic mean (standard error)	48 (± 3)	50 (± 3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Evolution of affected disc(s) by quantitative Magnetic Resonance Imaging (RMI): Density Before transplantation

End point title	Evolution of affected disc(s) by quantitative Magnetic Resonance Imaging (RMI): Density Before transplantation

End point description:

To homogenize the results of different patients, the water content values of the affected discs were normalized to the values obtained from the healthy discs in the same individual; for these purposes, the density of the affected segments was divided by the average value of the healthy discs. Finally, the value after the treatment was divided by the baseline value.

End point type	Secondary

End point timeframe:

Before intervention

End point values	Experimental	Active Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: units				
arithmetic mean (standard error)	0.46 (± 0.05)	0.48 (± 0.05)		

Statistical analyses

No statistical analyses for this end point

Secondary: Evolution of affected disc(s) by quantitative Magnetic Resonance Imaging (RMI): Density at 6 months

End point title	Evolution of affected disc(s) by quantitative Magnetic Resonance Imaging (RMI): Density at 6 months

End point description:

Measurement of the amount of luid in the disc. To homogenize the results of different patients, the water content values of the affected discs were normalized to the values obtained from the healthy discs in the same individual; for these purposes, the density of the affected segments was divided by the average value of the healthy discs. Finally, the value after the treatment was divided by the baseline value.

End point type	Secondary

End point timeframe:

6 months after intervention

End point values	Experimental	Active Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: units				
arithmetic mean (standard error)	0.42 (± 0.05)	0.51 (± 0.05)		

Statistical analyses

No statistical analyses for this end point

Secondary: Evolution of affected disc(s) by quantitative RMI: Density at 12 months

End point title	Evolution of affected disc(s) by quantitative RMI: Density at 12 months

End point description:

To homogenize the results of different patients, the water content values of the affected discs were normalized to the values obtained from the healthy discs in the same individual; for these purposes, the density of the affected segments was divided by the average value of the healthy discs. Finally, the value after the treatment was divided by the baseline value.

End point type	Secondary

End point timeframe:

12 months after intervention

End point values	Experimental	Active Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: units				
arithmetic mean (standard error)	0.52 (± 0.06)	0.49 (± 0.05)		

Statistical analyses

No statistical analyses for this end point

Secondary: SF-12 Physical Component: Baseline

End point title	SF-12 Physical Component: Baseline

End point description:

Results from the physical component of the short form-12 (SF-12) life quality questionnaire measured before the intervention.

End point type	Secondary

End point timeframe:

Before intervention

End point values	Experimental	Active Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: units				
arithmetic mean (standard error)	39 (± 2)	40 (± 3)		

Statistical analyses

No statistical analyses for this end point

Secondary: SF-12 Mental Component: Baseline

End point title	SF-12 Mental Component: Baseline
End point description:	

Results from the mental component of the short form-12 (SF-12) life quality questionnaire measured before the intervention.

End point type	Secondary
End point timeframe:	

Before intervention

End point values	Experimental	Active Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: units				
arithmetic mean (standard error)	46 (± 3)	52 (± 3)		

Statistical analyses

No statistical analyses for this end point

Secondary: VAS-Baseline

End point title	VAS-Baseline
End point description:	

Pain evaluation using a visual analogue scale (VAS) at baseline. Outcomes are expressed using a 0%-100% escale.

End point type	Secondary
End point timeframe:	

Before the intervention

End point values	Experimental	Active Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: percent				
arithmetic mean (standard error)	67 (± 7)	62 (± 7)		

Statistical analyses

No statistical analyses for this end point

Secondary: VAS-3 months

End point title	VAS-3 months

End point description:

Subject's pain evaluation using a visual analogue scale (VAS) 3 months after intervention. Outcomes are expressed using a 0%-100% escale.

End point type	Secondary

End point timeframe:

3 months after intervention

End point values	Experimental	Active Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: percent				
arithmetic mean (standard error)	43 (± 9)	46 (± 8)		

Statistical analyses

No statistical analyses for this end point

Secondary: VAS-6 months

End point title	VAS-6 months

End point description:

Subject's pain evaluation using a visual analogue scale (VAS) 6 months after intervention. Outcomes are expressed using a 0%-100% escale.

End point type	Secondary

End point timeframe:

6 months after intervention

End point values	Experimental	Active Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: percent				
arithmetic mean (standard error)	40 (± 8)	51 (± 8)		

Statistical analyses

No statistical analyses for this end point

Secondary: VAS-12 months

End point title	VAS-12 months
End point description:	

Subject's pain evaluation using a visual analogue scale (VAS) 12 months after intervention. Outcomes are expressed using a 0%-100% escale.

End point type	Secondary
End point timeframe:	

12 months after intervention

End point values	Experimental	Active Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: percent				
arithmetic mean (standard error)	47 (± 10)	47 (± 8)		

Statistical analyses

No statistical analyses for this end point

Secondary: ODI: Baseline

End point title	ODI: Baseline
End point description:	

Subject's Disability score in the Oswestry Disabiility Index (ODI) before intervention. Outcomes are expressed using a 0%-100% escale.

End point type	Secondary
End point timeframe:	

Before intervention

End point values	Experimental	Active Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: percent				
arithmetic mean (standard error)	34 (± 7)	24 (± 4)		

Statistical analyses

No statistical analyses for this end point

Secondary: ODI: 3 months

End point title	ODI: 3 months

End point description:

Subject's Disability score in the Oswestry Disabiility Index (ODI) 3 months after intervention. Outcomes are expressed using a 0%-100% escale.

End point type	Secondary

End point timeframe:

3 months after intervention

End point values	Experimental	Active Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: percent				
arithmetic mean (standard error)	16 (± 6)	25 (± 4)		

Statistical analyses

No statistical analyses for this end point

Secondary: ODI: 6 months

End point title	ODI: 6 months

End point description:

Subject's Disability score in the Oswestry Disabiility Index (ODI) 6 months after intervention. Outcomes are expressed using a 0%-100% escale.

End point type	Secondary

End point timeframe:

6 months after intervention

End point values	Experimental	Active Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: percent				
arithmetic mean (standard error)	20 (± 7)	30 (± 6)		

Statistical analyses

No statistical analyses for this end point

Secondary: ODI: 12 months

End point title	ODI: 12 months

End point description:

Subject's Disability score in the Oswestry Disabiility Index (ODI) 12 months after intervention. Outcomes are expressed using a 0%-100% escale.

End point type	Secondary

End point timeframe:

12 months after intervention.

End point values	Experimental	Active Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: percent				
arithmetic mean (standard error)	22 (± 7)	34 (± 7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pfirrman stage: 6 months

End point title	Pfirrman stage: 6 months

End point description:

Assessment of nucleus pulposus evolution by Pfirrmann grading (1 to 5), which takes into account the structure of the disc, the distinction of nucleus pulposus and annulus fibrosus, the signal intensity and the height of the disc.
Evolution of the variable 6 months after intervention.

End point type	Secondary

End point timeframe:

6 months after intervention

End point values	Experimental	Active Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: unit(s)				
arithmetic mean (standard deviation)	3.38 (± 0.15)	3.55 (± 0.18)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pfirrman stage: 12 months

End point title	Pfirrman stage: 12 months

End point description:

Assessment of nucleus pulposus evolution by Pfirrmann grading (1 to 5), which takes into account the structure of the disc, the distinction of nucleus pulposus and annulus fibrosus, the signal intensity and the height of the disc.
Evolution of the variable 12 months after the intervention.

End point type	Secondary

End point timeframe:

12 months after intervention

End point values	Experimental	Active Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: units				
arithmetic mean (standard error)	3.18 (± 0.17)	3.78 (± 0.16)		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Pfirrman stage: Baseline

End point title	Pfirrman stage: Baseline

End point description:

Assessment of nucleus pulposus evolution by Pfirrmann grading (1 to 5), which takes into account the structure of the disc, the distinction of nucleus pulposus and annulus fibrosus, the signal intensity and the height of the disc.

End point type	Post-hoc

End point timeframe:

Before intervention

End point values	Experimental	Active Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: unit(s)				
arithmetic mean (standard error)	3.68 (± 0.13)	3.15 (± 0.15)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:	
Adverse events reporting started when the patient signed the Informed Consent from, and lasted up to the last visit of each patient.	
Adverse event reporting additional description:	
Only those events that were registered after the intervention were considered as Treatment emergent Adverse Events and reported.	
Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Experimental
Reporting group description:	
12 patients were randomly allocated to this arm and received allogeneic bone marrow MSCs by intradiscal injection of 25×10e6 cells per segment under local anesthesia.	
Reporting group title	Control
Reporting group description:	
12 patients were randomly assigned to the control group. All the procedures were the same than the Experimental arm. The control group received a sham infiltration of paravertebral musculature with the anesthetic.	

Serious adverse events	Experimental	Control	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
General disorders and administration site conditions			
Device failure			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Experimental	Control	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 12 (41.67%)	9 / 12 (75.00%)	
Musculoskeletal and connective tissue disorders			

Back pain		
subjects affected / exposed	5 / 12 (41.67%)	9 / 12 (75.00%)
occurrences (all)	8	13

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.

Further studies shall track the long-term evolution as well as investigate the anatomical and functional changes that occur in the intervertebral spaces and shall increase the number of patients, which was an important limitation of the present study

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/27661661