Clinical trial results:
A phase I-IIa safety and efficacy pilot clinical trial of intraarticular administration of autologous mesenchymal stem cells in meniscus injury

Summary

EudraCT number	2011-006270-13
Trial protocol	ES
Global end of trial date	04 March 2017

Results information

Result version number	v1 (current)
This version publication date	29 March 2022
First version publication date	29 March 2022
Summary attachment (see zip file)	A Phase I-IIa Safety and Efficacy Pilot Clinical Trial of Intraarticular Administration of Autologous Mesenchymal Cells for Meniscus Injury (SYNOPSIS (Meniscus injury).pdf)

Trial information

Trial identification

Sponsor protocol code	XCEL-MEN-01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02033525
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Banc de Sang i Teixits
Sponsor organisation address	Passeig Taulat 116, Barcelona, Spain,
Public contact	Ruth Coll, Banc de Sang i Teixits, +34 935573500, rucoll@bst.cat
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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	04 March 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 March 2017
Global end of trial reached?	Yes
Global end of trial date	04 March 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To assess the efficacy of intraarticular administration of XCEL-M-ALPHA by VAS for pain at 12 month follow-up.

Protection of trial subjects:

Patients were able to contact the investigator whenever needed, in order to proceed with the most adequate approach to the reported issue.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 December 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: 21
Worldwide total number of subjects	21
EEA total number of subjects	21

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)	21
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited between January 2014 and May 2016 , from those patients visited at ICATME (Dexeus Hospital), in Barcelona, Spain.

Pre-assignment

Screening details:

All screened patients entered the study. There were no screening failure.

Pre-assignment period milestones

Number of subjects started	21
Number of subjects completed	21

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	BM-MSC

Arm description:

The patients assigned to the experimental treatment were scheduled for the previous extraction of BM and, after the days necessary for cell expansion, the mesenchymal cells were infiltrated in the knee by intra-articular puncture.

Arm type	Experimental
Investigational medicinal product name	BM-MSC
Investigational medicinal product code	
Other name	Autologous mesenchymal stromal cells from bone marrow
Pharmaceutical forms	Injection/infusion
Routes of administration	Intraarticular use

Dosage and administration details:

Dose: 40x106 ± 10x106 mesenchymal cells in approximately 6 ml suspension.
Pharmaceutical form: Suspension for intraarticular infiltration in a prefilled syringe
Administration route: Intraarticular
Treatment administration schedule: Single dose
Lot number: Autologous product with a unique lot number for each one of the 10 productions

Arm title	Rehabilitation

Arm description:

The control group followed conservative treatment through the same rehabilitation program

Arm type	Rehabilitation

No investigational medicinal product assigned in this arm

Number of subjects in period 1	BM-MSC	Rehabilitation
Started	10	11
Completed	10	11

Baseline characteristics

Reporting groups	
Reporting group title	BM-MSC
Reporting group description:	
The patients assigned to the experimental treatment were scheduled for the previous extraction of BM and, after the days necessary for cell expansion, the mesenchymal cells were infiltrated in the knee by intra-articular puncture.	
Reporting group title	Rehabilitation
Reporting group description:	
The control group followed conservative treatment through the same rehabilitation program	

Reporting group values	BM-MSC	Rehabilitation	Total
Number of subjects	10	11	21
Age categorical Units: Subjects			
40-60 years			0
Age continuous			
Min; Max (SD) rehabilitation group: 40;60 (6.8) Min; Max (SD) experimental group: 39;58 (6.1)			
Units: years			
arithmetic mean	49.2	47.9	
standard deviation	± 6.1	± 6.8	-
Gender categorical Units: Subjects			
Female	1	3	4
Male	9	8	17

End points

End points reporting groups

Reporting group title	BM-MSC

Reporting group description:

The patients assigned to the experimental treatment were scheduled for the previous extraction of BM and, after the days necessary for cell expansion, the mesenchymal cells were infiltrated in the knee by intra-articular puncture.

Reporting group title	Rehabilitation

Reporting group description:

The control group followed conservative treatment through the same rehabilitation program

Primary: VAS for pain

End point title	VAS for pain

End point description:

Visual analogue scale (VAS) for pain at 12 month follow-up

End point type	Primary

End point timeframe:

12 month follow-up

End point values	BM-MSC	Rehabilitation		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: cm				
number (not applicable)	10	10		

Statistical analyses

Statistical analysis title	Main variable for efficacy (VAS for pain at 12m)

Statistical analysis description:

Efficacy analysis was performed by intention to treat, using the FAS analysis set. In case of missing values (missings), these were replaced by the last available value (Last Observation Carried Forward or LOCF), even if this was the baseline. In this case, as well as in the case of important protocol violations, the convenience of conducting sensitivity analysis without imputation of missing data, or excluding said violations, was assessed.

Comparison groups	BM-MSC v Rehabilitation
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.19
Method	t-test, 2-sided

Notes:

[1] - Greater percentage changes were observed in the BM-MSC group than in the group of rhb, but were not statistically significant, which could be attributed to the low sample size, to the dispersion of results obtained or to the high number of missing data.

For changes in the VAS for pain at 12 m, the adjusted mean estimates (least-squares) showed a slightly greater percentage reduction in the BM-MSC group (-67.46) than in the rhb group (-44.33) (not statistically significant)

Secondary: Efficacy by MRI

End point title	Efficacy by MRI

End point description:

Efficacy will be assessed by qualitative and quantitative changes of the meniscus and articular cartilage by imaging procedures (MRI) T2 mapping at 6 and 12 month follow-up.

End point type	Secondary

End point timeframe:

6 and 12 month follow-up.

End point values	BM-MSC	Rehabilitation		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: mseg				
number (not applicable)	10	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical efficacy by clinical questionnaires

End point title	Clinical efficacy by clinical questionnaires

End point description:

IKDC, KOOS and Lysholm functionality test and SF-36 quality of life at 3, 6 and 12 month follow-up

End point type	Secondary

End point timeframe:

3, 6 and 12 month follow-up

End point values	BM-MSC	Rehabilitation		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: none				
number (not applicable)	10	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Safety

End point title	Safety

End point description:

Safety will be assessed by collecting adverse events, physical exam, laboratory tests, and vital signs

End point type	Secondary

End point timeframe:

12 month follow-up

End point values	BM-MSC	Rehabilitation		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	11		
Units: none				
number (not applicable)	10	11		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From the iIC signature to the 12-months follow-up	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0
Reporting groups	
Reporting group title	BM-MSC
Reporting group description: -	
Reporting group title	Rehabilitation
Reporting group description: -	

Serious adverse events	BM-MSC	Rehabilitation	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 10 (10.00%)	1 / 11 (9.09%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Musculoskeletal and connective tissue disorders			
Neck pain	Additional description: Experimental group. Not related to the study medication		
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle mass	Additional description: Control grup. Not related to the study medication		
subjects affected / exposed	0 / 10 (0.00%)	1 / 11 (9.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	BM-MSC	Rehabilitation	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 10 (90.00%)	7 / 11 (63.64%)	
Investigations			

Blood cholesterol abnormal			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Procedural pain	Additional description: Pain related to BM extraction		
subjects affected / exposed	3 / 10 (30.00%)	0 / 11 (0.00%)	
occurrences (all)	3	0	
Epicondylitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Ligament sprain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 10 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Application site joint pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 10 (40.00%)	3 / 11 (27.27%)	
occurrences (all)	4	3	
Muscle atrophy			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Bursitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Back pain			
subjects affected / exposed	2 / 10 (20.00%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Tendon pain			

subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Patellofemoral pain syndrome			
subjects affected / exposed	2 / 10 (20.00%)	2 / 11 (18.18%)	
occurrences (all)	2	2	

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.

Limited sample size. Premature study discontinuations were significantly more frequent in the rehabilitation group than in the experimental group (7/10 vs 1/10 patients respectively, p = 0.022), most of them due to therapeutic ineffectiveness.

Notes: