Clinical trial results:
A phase IIa, unicenter, prospective, randomized, parallel, two-arms, single-dose, open-label with blinded assessor pilot clinical trial to assess ex vivo expanded adult autologous mesenchymal stromal cells fixed in allogeneic bone tissue (XCEL-MT-OSTEO-ALPHA) in non hypertrphic pseudoarthrosis of long bones

Summary

EudraCT number	2013-005025-23
Trial protocol	ES
Global end of trial date	20 December 2019

Results information

Result version number	v1 (current)
This version publication date	18 May 2022
First version publication date	18 May 2022
Summary attachment (see zip file)	A Phase IIa, Single Center, Prospective, Randomized, Parallel, Two-arms, Single-dose, Open-label With Blinded Assessor Pilot Clinical Trial to Assess ex Vivo Expanded Adult Autologous Mesenchymal Stro (CSR Synopsis.pdf)

Trial information

Trial identification

Sponsor protocol code	XCEL-PSART-01

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Banc de Sang i Teixits
Sponsor organisation address	Passeig Taulat 116, Barcelona, Spain, 08005
Public contact	Ruth Coll Bonet, Responsible for Clinical Development, Banc de Sang i Teixits (BST), +34 935573500, rucoll@bst.cat
Scientific contact	Ruth Coll Bonet, Responsible for Clinical Development, Banc de Sang i Teixits (BST), +34 935573500, rucoll@bst.cat

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	05 March 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 March 2019
Global end of trial reached?	Yes
Global end of trial date	20 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

-To assess the efficacy of XCEL-MT-OSTEO-ALPHA in the treatment of non-hypertrophic pseudarthrosis of long bones through quantifying of the Hounsfield units by TC at month 12 postreatment.

Protection of trial subjects:

Patients were sedated and locally anesthesied for the bone marrow extraction and were discharged after recovery.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 January 2015
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: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	20
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited between January 2015 and February 2018 in a single centre (Hospital ASEPEYO Sant Cugat (Barcelona)).

Pre-assignment

Screening details:

Patients between 18 and 65 years of age affected with acquired metaphysodiaphyseal non-hypertrophic pseudoarthrosis of long bones, visited at Hospital ASEPEYO Sant Cugat (Barcelona)

Period 1

Period 1 title	Period 1 (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor[1]

Blinding implementation details:

As the tested product is from autologous bone marrow meaning randomised patients had to undergo for a previous bone marrow extraction, the only person that could be blinded was the radiologist who assessed the radiological images.

Arms

Are arms mutually exclusive?	Yes
Arm title	XCEL-MT-OSTEO-ALPHA

Arm description:

Mechanical stabilization and XCEL-MT-OSTEO-ALPHA (ex Vivo Expanded Adult Autologous Mesenchymal Stromal Cells Fixed in Allogeneic Bone Tissue).

Arm type	Experimental
Investigational medicinal product name	XCEL-MT-OSTEO-ALPHA
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Local use

Dosage and administration details:

Product: XCEL-MT-OSTEO-ALPHA
- Dose: 3x105 y 1x106 mesenchymal stromal cells per cubic centimeter of bone (5 or 10 cc)
- Pharmaceutical form: Solid particles.
- Administration route: Surgically implanted
- Administration periodicity: Single dose.

Arm title	Standar of care

Arm description:

Mechanical stabilization and autologous graft

Arm type	Active comparator
Investigational medicinal product name	Autologous graft
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Local use

Dosage and administration details:

Autologous graft. Dosage is not applicable.

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Being an autologous treatment requiring previous bone marrow extraction, the only person that could be blind was the radiologist.

Number of subjects in period 1	XCEL-MT-OSTEO-ALPHA	Standar of care
Started	10	10
Completed	10	10

Baseline characteristics

Reporting groups	
Reporting group title	XCEL-MT-OSTEO-ALPHA
Reporting group description:	
Mechanical stabilization and XCEL-MT-OSTEO-ALPHA (ex Vivo Expanded Adult Autologous Mesenchymal Stromal Cells Fixed in Allogeneic Bone Tissue).	
Reporting group title	Standar of care
Reporting group description:	
Mechanical stabilization and autologous graft	

Reporting group values	XCEL-MT-OSTEO-ALPHA	Standar of care	Total
Number of subjects	10	10	20
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	10	10	20
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	43.7	51.8	
standard deviation	± 9.9	± 7.9	-
Gender categorical Units: Subjects			
Female	1	2	3
Male	9	8	17

End points

End points reporting groups	
Reporting group title	XCEL-MT-OSTEO-ALPHA
Reporting group description:	
Mechanical stabilization and XCEL-MT-OSTEO-ALPHA (ex Vivo Expanded Adult Autologous Mesenchymal Stromal Cells Fixed in Allogeneic Bone Tissue).	
Reporting group title	Standar of care
Reporting group description:	
Mechanical stabilization and autologous graft	

Primary: Change in mean percentage of Housfield Units by CT	
End point title	Change in mean percentage of Housfield Units by CT
End point description:	
End point type	Primary
End point timeframe:	
12 months	

End point values	XCEL-MT-OSTEO-ALPHA	Standar of care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	8		
Units: percent				
arithmetic mean (standard deviation)	46 (± 19.25)	54.39 (± 21.63)		

Statistical analyses

Statistical analysis title	Change in mean percentage of HU
Comparison groups	XCEL-MT-OSTEO-ALPHA v Standar of care
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4835
Method	Regression, Linear

Statistical analysis title	Change in mean percentage of HU
Comparison groups	Standar of care v XCEL-MT-OSTEO-ALPHA

Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4835
Method	Regression, Linear

Secondary: Change in mean percentage of Housfield Units by CT

End point title	Change in mean percentage of Housfield Units by CT
End point description:	

End point type	Secondary
End point timeframe:	
6 months	

End point values	XCEL-MT-OSTEO-ALPHA	Standar of care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	8		
Units: percent				
arithmetic mean (standard deviation)	29.70 (± 13.86)	40.50 (± 19.88)		

Statistical analyses

Statistical analysis title	Change in mean percentage of HU
Comparison groups	XCEL-MT-OSTEO-ALPHA v Standar of care
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3761
Method	Regression, Linear

Secondary: Degree of consolidation according to TUS scale (Tomographic union Score)

End point title	Degree of consolidation according to TUS scale (Tomographic union Score)
End point description:	

End point type	Secondary
End point timeframe:	
6 months	

End point values	XCEL-MT-OSTEO-ALPHA	Standar of care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	8		
Units: Units				
Consolidated	1	5		
Not consolidated	7	3		

Statistical analyses

Statistical analysis title	degree of consolidation according to TUS scale
Comparison groups	XCEL-MT-OSTEO-ALPHA v Standar of care
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.119
Method	Fisher exact

Secondary: Degree of consolidation according to TUS scale (Tomographic union Score)

End point title	Degree of consolidation according to TUS scale (Tomographic union Score)

End point description:

End point type	Secondary

End point timeframe:

12 months

End point values	XCEL-MT-OSTEO-ALPHA	Standar of care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	8		
Units: Units				
Consolidated	3	6		
Not consolidated	4	2		

Statistical analyses

Statistical analysis title	degree of consolidation according to TUS scale
Comparison groups	XCEL-MT-OSTEO-ALPHA v Standar of care
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.315
Method	Fisher exact

Secondary: Degree of consolidation according to RUS scale (Radiograhic Union Score)

End point title	Degree of consolidation according to RUS scale (Radiograhic Union Score)

End point description:

End point type	Secondary

End point timeframe:

6 months

End point values	XCEL-MT-OSTEO-ALPHA	Standar of care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	8		
Units: Units				
Consolidated	4	5		
Not Consolidated	4	3		

Statistical analyses

Statistical analysis title	degree of consolidation according to RUS scale
Comparison groups	XCEL-MT-OSTEO-ALPHA v Standar of care
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Fisher exact

Secondary: Degree of consolidation according to RUS scale (Radiograhic Union Score)

End point title	Degree of consolidation according to RUS scale (Radiograhic Union Score)

End point description:

End point type	Secondary
End point timeframe: 12 months	

End point values	XCEL-MT-OSTEO-ALPHA	Standar of care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	8		
Units: Units				
Consolidated	5	7		
Not consolidated	2	1		

Statistical analyses

Statistical analysis title	degree of consolidation according to RUS scale
Comparison groups	XCEL-MT-OSTEO-ALPHA v Standar of care
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.569
Method	Fisher exact

Secondary: Changes in the EUROQoL-5D

End point title	Changes in the EUROQoL-5D
End point description: 	
End point type	Secondary
End point timeframe: 6 months	

End point values	XCEL-MT-OSTEO-ALPHA	Standar of care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	8		
Units: mean				
arithmetic mean (standard deviation)	0.6217 (± 0.2248)	0.5451 (± 0.1931)		

Statistical analyses

Statistical analysis title	Changes in punctuation on the Euroqol-5D
Comparison groups	XCEL-MT-OSTEO-ALPHA v Standar of care
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3708
Method	Regression, Linear

Secondary: Changes in the EUROQoL-5D	
End point title	Changes in the EUROQoL-5D
End point description:	
End point type	Secondary
End point timeframe:	
12 months	

End point values	XCEL-MT-OSTEO-ALPHA	Standar of care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	7		
Units: mean				
arithmetic mean (standard deviation)	0.5795 (± 0.1782)	0.7176 (± 0.2060)		

Statistical analyses

Statistical analysis title	Changes in the EUROQoL-5D
Comparison groups	XCEL-MT-OSTEO-ALPHA v Standar of care
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4204
Method	Regression, Linear

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were collected from the signature of the informed consent form to the end of the trial

Adverse event reporting additional description:

Safety analyzes were performed with the available data, without using missing data imputation techniques.
The analysis techniques were descriptive, including graphs and individual data listings. The AE were described by means of lists of the AE, organized by treatment group and patient, which included the preferred terms (MedDRA), as well as the c

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	XCEL-MT-OSTEO-ALPHA

Reporting group description:

Patients randomized to XCEL-MT-OSTEO-ALPHA

Reporting group title	STANDARD OF CARE

Reporting group description:

Patients randomized to standard of care treatment (autologous iliac creast)

Serious adverse events	XCEL-MT-OSTEO-ALPHA	STANDARD OF CARE	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 10 (30.00%)	2 / 10 (20.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
General disorders and administration site conditions			
Medical device site joint pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Pseudarthrosis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
postprocedural infection			

subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device breakage			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	XCEL-MT-OSTEO-ALPHA	STANDARD OF CARE	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 10 (50.00%)	4 / 10 (40.00%)	
Injury, poisoning and procedural complications			
Post procedural discomfort			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Limb operation			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dysaesthesia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Hypoaesthesia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Medical device site discomfort			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	
occurrences (all)	1	2	
Discomfort			

subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Gait disturbance			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Medical device site joint discomfort			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Medical device site pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Haemorrhoids			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Encopresis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Musculoskeletal discomfort			
subjects affected / exposed	3 / 10 (30.00%)	1 / 10 (10.00%)	
occurrences (all)	3	1	
Pain in extremity			
subjects affected / exposed	3 / 10 (30.00%)	1 / 10 (10.00%)	
occurrences (all)	3	1	
Back pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Muscle atrophy			

subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Muscle contracture			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Tendonitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Infections and infestations			
Cystitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Viral infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 September 2015	The dose to be used in this study was increased from 10 to 20 cc, with a minimum cell content of 30x105 and a maximum of 20x106

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported