Clinical trial results:
A pivotal Phase IIb/III, multicentre, randomised, open, controlled study on the efficacy and safety of autologous osteoblastic cells (PREOB®) implantation in non-infected hypotrophic non-union fractures.

Summary

EudraCT number	2011-005584-24
Trial protocol	BE NL
Global end of trial date	26 March 2019

Results information

Result version number	v1 (current)
This version publication date	02 November 2019
First version publication date	02 November 2019
Summary attachment (see zip file)	synoptic clinical sudy report (20190410 _BT_PREOBNU3_Clinical Study Report_Synoptic_Final_EudraCT.pdf)

Trial information

Trial identification

Sponsor protocol code	PREOB-NU3

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bone Theapeutics S.A.
Sponsor organisation address	rue Auguste Picard 37, Gosselies, Belgium, B-6041
Public contact	Clinical Trial Information, Bone Therapeutics S.A., preob.nu3@bonetherapeutics.com
Scientific contact	Clinical Trial Information, Bone Therapeutics S.A., preob.nu3@bonetherapeutics.com

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	10 May 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 April 2016
Global end of trial reached?	Yes
Global end of trial date	26 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objectives of the study are to demonstrate the non-inferiority of PREOB® implantation over bone autograft in terms of safety and efficacy at Month 12 clinically on the basis of the global disease evaluation score (as assessed by visual analogue scales) and radiologically on the basis of the percentage of patients with radiological improvement as assessed by RUST score determined by CT Scan.

Protection of trial subjects:

GCP

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 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	Belgium: 5
Worldwide total number of subjects	5
EEA total number of subjects	5

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)	5
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The PREOB-NU3 study was terminated early (25 September 2017 (Belgium (BE) / 17 July 2015 (France (FR); Study termination for refusal of study extension by CCP) / 22 Augustus 2016 (The Netherlands (NL)) by the sponsor with <10% of planned subject enrolled because of recruitment difficulties.

Pre-assignment

Screening details:

Of the 16 subjects enrolled in the study, 9 (56.25%) subjects were screen failure

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Preob

Arm description:

Test item

Arm type	Experimental
Investigational medicinal product name	Preob
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intralesional use

Dosage and administration details:

Single dose, 4 x 10exp6 cells/mL

Arm title	Bone autograft

Arm description:

Active comparator

Arm type	Active comparator
Investigational medicinal product name	Bone autograft
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intralesional use

Dosage and administration details:

Bone autograft

Number of subjects in period 1	Preob	Bone autograft
Started	2	3
Completed	2	3

Baseline characteristics

Reporting groups	
Reporting group title	Preob
Reporting group description: Test item	
Reporting group title	Bone autograft
Reporting group description: Active comparator	

Reporting group values	Preob	Bone autograft	Total
Number of subjects	2	3	5
Age categorical Units: Subjects			
Adult	2	3	5
Age continuous Units: years arithmetic mean standard deviation	 37.2 ± 7.3	 45.7 ± 10.3	 -
Gender categorical Units: Subjects			
Female	0	1	1
Male	2	2	4

Subject analysis sets	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description: Safety and efficacy population	

Reporting group values	ITT		
Number of subjects	5		
Age categorical Units: Subjects			
Adult	5		
Age continuous Units: years arithmetic mean standard deviation	 42.32 ± 9.4		
Gender categorical Units: Subjects			
Female	1		
Male	4		

End points

End points reporting groups

Reporting group title	Preob
Reporting group description: Test item	
Reporting group title	Bone autograft
Reporting group description: Active comparator	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description: Safety and efficacy population	

Primary: Achievement of Union

End point title	Achievement of Union[1]
End point description: Achievement of fracture healing (union)	
End point type	Primary
End point timeframe: 12 months	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The study was interrupted and no analysis of efficacy was performed

End point values	Preob	Bone autograft	ITT	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	2	3	5	
Units: Patient	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: 24 months	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	2.1

Reporting groups	
Reporting group title	Preob
Reporting group description: Test	
Reporting group title	Bone autograft
Reporting group description: Active comparator	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: The non-serious adverse events will be filled in at a later stage

Serious adverse events	Preob	Bone autograft	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	2 / 3 (66.67%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post-traumatic pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Medical device change			

subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 2 (0.00%)	2 / 3 (66.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Preob	Bone autograft	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	

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? Yes

Date	Interruption	Restart date
25 September 2017	the clinical trial was prematurely stoped to focus resources in the allogeneic platform and provide optimal value for patients	-

Notes:

Limitations and caveats

None reported