Clinical trial results:
A Pilot Phase IIa, Multicentre, Open, Proof-of-concept Study on the Safety and the Efficacy of Allogeneic Osteoblastic Cells (ALLOB®) Implantation in Rescue Interbody Fusion

Summary

EudraCT number	2014-002416-16
Trial protocol	BE
Global end of trial date	25 May 2020

Results information

Result version number	v1 (current)
This version publication date	14 November 2021
First version publication date	14 November 2021

Trial information

Trial identification

Sponsor protocol code	ALLOB-RIF1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02328287
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bone Therapeutics S.A.
Sponsor organisation address	Rue Auguste Piccard, 37, Gosselies, Belgium, 6041
Public contact	Clinical Trial Information, Bone Therapeutics S.A., regulatory@bonetherapeutics.com
Scientific contact	Clinical Trial Information, Bone Therapeutics S.A., regulatory@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	26 March 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 March 2020
Global end of trial reached?	Yes
Global end of trial date	25 May 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to assess the safety and efficacy of ALLOB® in rescue interbody fusion over 12 months in patients suffering from failed lumbar fusion at one or two level(s).

Safety:
At each visit, subjects will be assessed for the potential occurrence of any AE or SAE related to the product or to the procedure, using patient open non-directive questionnaires, vital signs and laboratory measurements.

Efficacy:
The efficacy of the treatment will be evaluated at Month 12:
- Radiologically (progression of the lumbar fusion): the Fusion Score as assessed by CT-scan vs. baseline.
- Clinically (functional disability): the changes in ODI 2.1a vs. baseline.

Protection of trial subjects:

Standard-of-care treatment.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 February 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	24 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 10
Worldwide total number of subjects	10
EEA total number of subjects	10

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)	9
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment period: 17 February 2015 - 17 March 2017
Country: Belgium

Pre-assignment

Screening details:

Men and women aged 18 years or more at the time of implantation, diagnosed with failed lumbar fusion at one or two level(s) of a minimum of 15 months following the interbody fusion, and requiring a rescue surgery.

Period 1

Period 1 title	Safety population (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	ALLOB

Arm description: -

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

Dosage and administration details:

One single administration of ALLOB (4mL - 100x10^6 cells) per lumbar level with a maximum of two treated levels

Number of subjects in period 1[1]	ALLOB
Started	6
Completed	5
Not completed	1
Consent withdrawn by subject	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Of the 10 patients enrolled in the study, 8 were eligible and 2 were screened failure.
Of the 8 eligible patients, 6 were treated and 2 were not due to technical issues during the implantation procedure.
The abbreviated CSR contains only the analysed data for the 6 treated patients.

Baseline characteristics

Reporting groups

Reporting group title	ALLOB

Reporting group description: -

Reporting group values	ALLOB	Total	
Number of subjects	6	6	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	6	6	
From 65-84 years	0	0	
85 years and over	0	0	
Not recorded	0	0	
Age continuous Units: years			
arithmetic mean	49.4		
standard deviation	± 9.58	-	
Gender categorical Units: Subjects			
Female	3	3	
Male	3	3	
Not recorded	0	0	

Subject analysis sets

Subject analysis set title	Safety population
Subject analysis set type	Safety analysis

Subject analysis set description:

All treated patients were included in the safety population.

Reporting group values	Safety population		
Number of subjects	6		
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 Not recorded	6		
Age continuous Units: years arithmetic mean standard deviation	 49.4 ± 9.58		
Gender categorical Units: Subjects			
Female Male Not recorded	3 3		

End points

End points reporting groups

Reporting group title	ALLOB
Reporting group description: -	
Subject analysis set title	Safety population
Subject analysis set type	Safety analysis
Subject analysis set description:	
All treated patients were included in the safety population.	

Primary: Changes in fusion score and ODI 2.1 vs. baseline

End point title	Changes in fusion score and ODI 2.1 vs. baseline[1]
End point description:	
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 early terminated. The low number of subjects treated (N=6) did not allow appropriate or meaningful statistical analysis of the ALLOB® efficacy data.

End point values	ALLOB	Safety population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	0[2]	0[3]		
Units: Patient				

Notes:

[2] - early termintation of the study

[3] - early termination of the study

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the treatment date till the end of long-term safety follow-up (36 months after the treatment)

Adverse event reporting additional description:

Open questionnaires, physical examination, vital signs, laboratory parameters, AEs/SAEs at each visit

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Safety population

Reporting group description: -

Serious adverse events	Safety population		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 6 (50.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Surgical and medical procedures			
Toe operation			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Central pain syndrome			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 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: 0 %

Non-serious adverse events	Safety population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)		
Investigations			
Blood calcium decreased			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Vitamin D decreased			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Patella fracture			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Rib fracture			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Vascular disorders			
Phlebitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Varicose vein			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Surgical and medical procedures			
Toe operation			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Wedge resection toenail			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Nervous system disorders			
Central pain syndrome			

subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Headache			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Sciatica			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Hiatus hernia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Stomatitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	6 / 6 (100.00%)		
occurrences (all)	7		

Musculoskeletal pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Neck pain			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Osteoarthritis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	3 / 6 (50.00%)		
occurrences (all)	3		
Periarthritis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Spinal pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Tendonitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	6		
Infection			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Pneumonia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Urinary tract infection			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	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

None reported