Clinical trial results:
A prospective randomised controlled trial on the use of BMP-7 (Bone Morphogenetic Protein-7) (OP-1®) and demineralised bone matrix (DBM) in tibial non-union.

Summary

EudraCT number	2006-006727-39
Trial protocol	BE
Global end of trial date	07 July 2012

Results information

Result version number	v1 (current)
This version publication date	11 October 2022
First version publication date	11 October 2022
Summary attachment (see zip file)	Statement of discontinuation (2006-006727-39.docx)

Trial information

Trial identification

Sponsor protocol code	AGO/2006/012

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Ghent University Hospital
Sponsor organisation address	Corneel Heymanslaan 10, Ghent, Belgium, 9000
Public contact	Hiruz CTU, Ghent University Hospital, +32 93320500, hiruz.ctu@uzgent.be
Scientific contact	Hiruz CTU, Ghent University Hospital, +32 93320500, hiruz.ctu@uzgent.be

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	07 July 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 July 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the clinical and radiological outcome of tibial diaphysary non-unions in patients surgically treated with adjunct use of BMP-7 compared to the adjunct use of demineralized bone matrix (DBM).

Protection of trial subjects:

Ethics review and approval, informed consent, supportive care and routine monitoring.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 October 2007
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: 2
Worldwide total number of subjects	2
EEA total number of subjects	2

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)	2
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

3 patients were screened from 18-10-2007 till 07-07-2012. 2 patients were enrolled. 2 patients were randomised.

Pre-assignment

Screening details:

Inclusion criteria:
- Diaphysary tibial non-unions will be included (minimum 9 months after first surgery)
- ASA 1 and ASA 2
- Gap length/bone contact detected (cms) (1-5 cm): largest cortical gap in any radiographic incidence
- Agrees to participate in post-operative evaluations and required rehabilitation regimen

Period 1

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

Blinding implementation details:

The evaluation of the radiographic images will be done by an independent blinded radiologist of the University Hospital of Ghent. The clinical observation of the primary endpoints a 9 months will be performed by an independent blinded clinician. The patient will be blinded as far as possible from group assignment. On several occasions the patient will be asked whether or not he knows what product was used on him. By this we will be able to monitor which patients remain blinded.

Arms

Are arms mutually exclusive?	Yes
Arm title	Control arm

Arm description:

Control group treated with allografts and Demineralised Bone Matrix (DBM).

Arm type	Active comparator
Investigational medicinal product name	Accell Plus
Investigational medicinal product code	
Other name	Demineralised Bone Matrix (DBM)
Pharmaceutical forms	Powder for implantation suspension
Routes of administration	Intraosseous use

Dosage and administration details:

Accell Plus (before: Connexus) is available in 1 ml; 2.5ml, 5 ml, 10 ml of gel or putty. It consists of 70% of human DBM (which is mainly collagen type 1) an 30 % polaxamer, a reverse phase medium that is more viscous at higher temperatures and improves handling. The polaxamer is quickly metabolised and renally excreted.
In this setting, use of 5 ml dose of Accell Plus and in some with bone defects of a larger size, the need may exist to use a 10 ml dose. This is the maximum quantity of DBM allowed in this study.

The product is placed directly in the dry fracture site after debridement during open surgery.

Arm title	Treatment arm

Arm description:

Treatment group treated with allografts and Morphogenetic Protein-7 (BMP-7) (OP-1®).

Arm type	Experimental

Investigational medicinal product name	Osigraft
Investigational medicinal product code	
Other name	BMP-7, OP-1
Pharmaceutical forms	Powder for implantation suspension
Routes of administration	Intraosseous use

Dosage and administration details:

Maximum of 2 doses
Total dose, 2 g gram(s)
Active substance: eptotermin alfa

The needed dose is prepared in a sterile manner and transferred to the sterile field. The product is placed directly in the dry fracture site after debridement during open surgery. Special attention is needed to make sure that the product is not irrigated away or sucked out.

Number of subjects in period 1	Control arm	Treatment arm
Started	1	1
Completed	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Control arm
Reporting group description: Control group treated with allografts and Demineralised Bone Matrix (DBM).	
Reporting group title	Treatment arm
Reporting group description: Treatment group treated with allografts and Morphogenetic Protein-7 (BMP-7) (OP-1®).	

Reporting group values	Control arm	Treatment arm	Total
Number of subjects	1	1	2
Age categorical Units: Subjects			
50	1	0	1
57	0	1	1
Gender categorical Units: Subjects			
Female	0	0	0
Male	1	1	2

End points

End points reporting groups

Reporting group title	Control arm
Reporting group description:	
Control group treated with allografts and Demineralised Bone Matrix (DBM).	
Reporting group title	Treatment arm
Reporting group description:	
Treatment group treated with allografts and Morphogenetic Protein-7 (BMP-7) (OP-1®).	

Primary: Repeated surgery

End point title	Repeated surgery[1]
End point description:	
End point type	Primary
End point timeframe:	
N/A	

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: No statistical analysis was done as only 2 patienst participated in the study

End point values	Control arm	Treatment arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	1		
Units: minor or major	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: (Surgical) complications

End point title	(Surgical) complications
End point description:	
End point type	Secondary
End point timeframe:	
N/A	

End point values	Control arm	Treatment arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	1		
Units: N/A	1	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
Overall study	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24

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

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: No non-serious adverse events were recorded for the participating patients.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 October 2006	Type of amendment: amendment to information in the CT application form, amendment to the protocol Reasons for the substantial amendment: changes in safety and integrity of trial subjects, changes in conduct or management of the trial Changes in inclusion criteria have been made: patient can be included into the study minimum 9 months after first surgery instead of 9 months after last major surgery.

Notes:

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.

This study was prematurely closed due to inclusion criteria that were too stringent.

Notes: