



Clinical trial results:

A phase III, randomized, controlled clinical pilot trial of lateral ridge augmentation using autogenous bone blocks or xenogenic bone block grafts loaded with recombinant human bone morphogenic protein 2

Summary

EudraCT number	2012-002002-46
Trial protocol	AT
Global end of trial date	15 March 2019

Results information

Result version number	v1 (current)
This version publication date	04 June 2020
First version publication date	04 June 2020

Trial information

Trial identification

Sponsor protocol code	2012-BMP1-2
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medical University of Graz
Sponsor organisation address	Billrothgasse 4, Graz, Austria, 8010
Public contact	Department für zahnärztl. Chirurgie, Universitätsklinik für Zahn-, Mund- und Kieferheilkunde, Med Uni Graz, 0043 31638513280, mi.payer@medunigraz.at
Scientific contact	Department für zahnärztl. Chirurgie, Universitätsklinik für Zahn-, Mund- und Kieferheilkunde, Med Uni Graz, 0043 31638513280, mi.payer@medunigraz.at

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	02 May 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 March 2019
Global end of trial reached?	Yes
Global end of trial date	15 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objective: To compare patient's perception and acceptance as well as efficacy of xenogenic bone block grafts loaded with rh-BMP-2 on bone quantity and quality 4 months after augmentation surgery to the gold standard (autogenous bone blocks).

Secondary objectives: Safety and tolerability of xenogenic bone block grafts loaded with rh- BMP-2 in regard of complications (soft-tissue/adverse effect) and the change in bone quantity over time.

Protection of trial subjects:

The study was conducted according to principles of Good Clinical Practice and approved by the local Ethics Committees.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 April 2013
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	Austria: 10
Country: Number of subjects enrolled	Switzerland: 15
Worldwide total number of subjects	25
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)	20
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment started in 2013 and the last study visit took place in 2019.

25 patients were included in total, one patient had to be excluded from the study. 24 patients completed the study.

Pre-assignment

Screening details:

In 23 out of 24 patients originally included, the augmentation procedure was considered to be successful. In one patient in the control group, the augmentation procedure failed. Since this patient refused to undergo another surgical procedure, he was excluded from the present study and replaced by an additional patient.

Period 1

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

Blinding implementation details:

Blinding of the study dentists and patients was not possible based on the nature of the study and the preparation involved (second surgery site in control group).

Arms

Are arms mutually exclusive?	Yes
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Arm title	Study group
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Arm description:

CE-marked medical device Bio-Oss Spongiosa Block® (xenogenic bone) loaded with InductOs® (1.5 mg Dibotermin alfa / ml) covered with Bio-Gide® (collagen membrane).

Arm type	Experimental
Investigational medicinal product name	InductOs
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dental gel
Routes of administration	Dental use

Dosage and administration details:

In the course of this study InductOs was implanted during dental augmentation surgery. InductOs (1,5 mg Dibotermin alfa) was applied to the CE-marked medical device Bio-Oss Spongiosa Block® (xenogenic bone) and covered with Bio-Gide®, a collagen membrane.

Arm title	Control group
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Arm description:

Autogenous bone block in combination with CE-marked medical device Bio-Oss® (xenogenic bone granules) covered with Bio-Gide® (collagen membrane).

Arm type	Medical device
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No investigational medicinal product assigned in this arm

Number of subjects in period 1	Study group	Control group
Started	12	13
Completed	12	12
Not completed	0	1
Consent withdrawn by subject	-	1

Baseline characteristics

Reporting groups

Reporting group title

Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	25	25	
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)	20	20	
From 65-84 years	5	5	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	8	8	
Male	17	17	

End points

End points reporting groups

Reporting group title	Study group
Reporting group description: CE-marked medical device Bio-Oss Spongiosa Block® (xenogenic bone) loaded with InductOs® (1.5 mg Dibotermin alfa / ml) covered with Bio-Gide® (collagen membrane).	
Reporting group title	Control group
Reporting group description: Autogenous bone block in combination with CE-marked medical device Bio-Oss® (xenogenic bone granules) covered with Bio-Gide® (collagen membrane).	

Primary: ridge width at the implant shoulder

End point title	ridge width at the implant shoulder
End point description:	
End point type	Primary
End point timeframe: 4 months after augmentation surgery	

End point values	Study group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: millimeters	12	12		

Statistical analyses

Statistical analysis title	Ridge width in mm
Statistical analysis description: The median ridge width increased from 4.0 mm (Q1 = 2.0; Q3 = 4.0) (test) and 2.0 mm (Q1 = 2.0; Q3 = 3.0) (control) to 7.0 mm (Q1 = 6.0; Q3 = 8.0) (test) and 7.0 mm (Q1 = 6.0; Q3 = 8.0) (control) at 4 months (intergroup p > .05). The differences between the groups were not statistically significant.	
Comparison groups	Study group v Control group
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	
P-value	≤ 0.05
Method	Wilcoxon (Mann-Whitney)

Secondary: Patient-reported outcome measures

End point title	Patient-reported outcome measures
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End point description:

The following parameters were analyzed:

pain during surgery recipient site

pain during surgery donor site

pain after surgery recipient site

pain after surgery donor site

swelling after surgery recipient site

swelling after surgery donor site

willingness to repeat treatment

There were no statistically significant differences, except for Pain during surgery at the recipient site in favour of the test group.

End point type	Secondary
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End point timeframe:

4 months

End point values	Study group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: Units on a scale	12	12		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Informed Consent to last patient's visit.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22
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Reporting groups

Reporting group title	All enrolled patients
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Reporting group description: -

Serious adverse events	All enrolled patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 25 (12.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
neoplasm of the prostate			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Stroke			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	All enrolled patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 25 (24.00%)		
Surgical and medical procedures			
Peri-implantitis			

subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		
Nervous system disorders Vertigo subjects affected / exposed occurrences (all) Paresthesia subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1 1 / 25 (4.00%) 1		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Fever subjects affected / exposed occurrences (all) Inflammation subjects affected / exposed occurrences (all) Minor chipping subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1 1 / 25 (4.00%) 1 1 / 25 (4.00%) 1 1 / 25 (4.00%) 1		
Musculoskeletal and connective tissue disorders Bone sequestrum subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 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