Clinical trial results:
The effect of systemic antibiotics on clinical and patient-centered outcomes of implant therapy and simultaneous guided bone regeneration. A randomised controlled clinical trial.

Summary

EudraCT number	2013-001811-56
Trial protocol	AT
Global end of trial date	30 April 2018

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	Syst.Antibiotics&GBR

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	Dept. of Oral Surgery & Radiology, PD. DDr. Michael Payer, 43 31638580659, mi.payer@medunigraz.at
Scientific contact	Dept. of Oral Surgery & Radiology, PD. DDr. Michael Payer, 43 31638580659, 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	15 May 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 April 2018
Global end of trial reached?	Yes
Global end of trial date	30 April 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of the present study was to determine the effect of a systemic antibiotic prophylaxis regime on patient-centred outcomes and postsurgical complications in patients undergoing oral implant therapy and simultaneous guided bone regeneration.

Protection of trial subjects:

Close monitoring of possible complications was implemented to ensure protection of trial subjects (4 follow-up visits after surgery).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 November 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	3 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Iceland: 22
Country: Number of subjects enrolled	China: 103
Country: Number of subjects enrolled	Singapore: 28
Country: Number of subjects enrolled	Austria: 59
Country: Number of subjects enrolled	Australia: 41
Worldwide total number of subjects	253
EEA total number of subjects	81

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)	177
From 65 to 84 years	76
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

253 patients were screened for the study in total.
17 primarily included cases had to be excluded due to heterogenous reasons. Thus at total of 236 cases were actually enrolled and analysed.

Pre-assignment

Screening details:

253 patients were screened for the study in total.
17 primarily included cases had to be excluded due to heterogenous reasons. Thus at total of 236 cases were analysed.
Randomisation into the two arms was performed at the time of consent

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Test group

Arm description:

Pre-operative antibiotics of 2 g amoxicillin were prescribed to the test group 1 hour prior to surgery and 500 mg thrice daily on days 1 to 3 after surgery.

Arm type	Experimental
Investigational medicinal product name	Amoxicillin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Pre-operative antibiotics of 2 g amoxicillin were prescribed to the test group 1 hour prior to surgery and 500 mg thrice daily on days 1 to 3 after surgery.

Arm title	Control group

Arm description:

The control group was given a placebo. Subjects were examined clinically by blinded examiners at 1, 2, 4 and 12 weeks from surgery for postoperative complications.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

In the control group a pre-operative placebo (containing corn starch) of 2 g was administered. An additional single dose of 500 mg of placebo was administered 8 hours after surgery and 500 mg thrice daily (8 hourly) on days 1 to 3 following implant placement and guided bone regeneration.

Number of subjects in period 1[1]	Test group	Control group
Started	117	119
Completed	117	119

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: 253 patients were initially screened but 236 cases were actually enrolled and analyzed.

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial
Reporting group description:	
Patients who signed informed consent and with complete data	

Reporting group values	Overall trial	Total	
Number of subjects	236	236	
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)	166	166	
From 65-84 years	70	70	
85 years and over	0	0	
Not recorded	0	0	
Gender categorical Units: Subjects			
Female	111	111	
Male	125	125	
Not recorded	0	0	

End points

End points reporting groups

Reporting group title	Test group
Reporting group description:	
Pre-operative antibiotics of 2 g amoxicillin were prescribed to the test group 1 hour prior to surgery and 500 mg thrice daily on days 1 to 3 after surgery.	
Reporting group title	Control group
Reporting group description:	
The control group was given a placebo. Subjects were examined clinically by blinded examiners at 1, 2, 4 and 12 weeks from surgery for postoperative complications.	

Primary: Patient-related outcome measures: pain, swelling, bruising, bleeding

End point title	Patient-related outcome measures: pain, swelling, bruising, bleeding
End point description:	
There was no statistically significant difference between the two treatment groups for bleeding, swelling, pain, and hematoma (all P > 0.05). However there was a significant time effect, where the mean VAS scores decreased over time (P < 0.001). However, no significant interaction effect between the treatment groups and time suggested that the decrease in the mean VAS scores in different treatment groups was not significantly different from each other for all the variables assessed. When adjusted for the center effect, consistent results were obtained that no statistically significant differences existed between the two treatment groups for all outcomes, but for a significant time effect (data not reported).	
End point type	Primary
End point timeframe:	
postoperative day 1-6, 7 & 14	

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	117	119		
Units: VAS score points	117	119		

Statistical analyses

Statistical analysis title	Outcome 1
Statistical analysis description:	
There was no statistically significant difference between the two Groups for bleeding, swelling, pain and hematoma (all p>0.05).	

Comparison groups	Control group v Test group

Number of subjects included in analysis	236
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	ANOVA

Statistical analysis title	Outcome 2

Statistical analysis description:

There was no statistically significant difference in flap closure, pain, swelling, pus, and implant stability of the Operation site between the two Groups (P>0.05).

Comparison groups	Test group v Control group
Number of subjects included in analysis	236
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	Chi-squared

Secondary: Presence of postsurgical complications

End point title	Presence of postsurgical complications

End point description:

There was no statistically significant difference in flap closure, pain, swelling, pus and implant stability of the operation site between the two treatment groups at any time (P > 0.05).

End point type	Secondary

End point timeframe:

1, 2, 4 and 12 weeks postoperatively

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From enrolment to study termination per patient

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22,0

Reporting groups

Reporting group title	Enrolled patients

Reporting group description: -

Serious adverse events	Enrolled patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 253 (0.79%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
General disorders and administration site conditions			
Multi-organ disorder			
subjects affected / exposed	1 / 253 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Acute anaphylactic reaction			
subjects affected / exposed	1 / 253 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Enrolled patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 253 (1.58%)		
Product issues			
Implant loss			

subjects affected / exposed occurrences (all)	4 / 253 (1.58%) 4		

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