Clinical trial results:
The Efficacy and Safety of Chlorhexidine Gluconate Chip (PerioChip®) in Therapy of Peri-implantitis

Summary

EudraCT number	2013-000383-28
Trial protocol	GB DE
Global end of trial date	26 June 2018

Results information

Result version number	v1 (current)
This version publication date	02 June 2021
First version publication date	02 June 2021
Summary attachment (see zip file)	CLI/016P Synopsis (CLI016P - Synopsis.pdf)

Trial information

Trial identification

Sponsor protocol code	CLI/016P

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02080403
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Dexcel Pharma Technologies Ltd
Sponsor organisation address	1 Dexcel St, Or-Akiva,, Israel, 3060000
Public contact	Dexcel Clinical Trial Information, Dexcel Pharma GmbH, 49 6023 94800,
Scientific contact	Dexcel Clinical Trial Information, Dexcel Pharma GmbH, 49 6023 94800,

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 October 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 June 2018
Global end of trial reached?	Yes
Global end of trial date	26 June 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of Chlorhexidine gluconate chip (PerioChip®) versus Subgingival debridement in Peri-implantitis patients.

Protection of trial subjects:

Informed consent, Patient confidentiality, Monitoring the participant closely during the study

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 August 2014
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	United Kingdom: 21
Country: Number of subjects enrolled	Germany: 23
Country: Number of subjects enrolled	Israel: 58
Country: Number of subjects enrolled	United States: 188
Worldwide total number of subjects	290
EEA total number of subjects	23

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)	156
From 65 to 84 years	131
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 10 sites: 6 in US, 2 in Isreal, 1 in Germany and 1 in UK

Pre-assignment

Screening details:

Study subjects had to meet the inclusion/exclusion criteria

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	Assessor[1]

Blinding implementation details:

The clinicians that performed the pocket measurments were blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	PerioChip

Arm description:

2.5 mg of chlorhexidine gluconate

Arm type	Experimental
Investigational medicinal product name	PerioChip
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Periodontal insert
Routes of administration	Dental use

Dosage and administration details:

Up to 2 PerioChips may have been inserted into each target implant, for a maximum chlorhexidine gluconate dosage of 5 mg per implant.
The maximum chlorhexidine gluconate dosage for a single patient across all implants was 10 mg (up to 4 PerioChips)

Arm title	Control

Arm description:

Mechanical Subgingival Debridement

Arm type	standart of care

No investigational medicinal product assigned in this arm

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: The study used a single-blind masking design, in which patients and clinicians responsible for administering treatment (ie, placing PerioChips in the periodontal pockets and/or performing subgingival debridement) were aware of treatment arm assignments but separate clinicians who were not aware of treatment arm assignments were responsible for performing the other study assessments.

Number of subjects in period 1	PerioChip	Control
Started	146	144
Completed	131	132
Not completed	15	12
Adverse event, serious fatal	2	2
Consent withdrawn by subject	5	1
Adverse event, non-fatal	4	2
Pregnancy	-	1
Lost to follow-up	2	-
Protocol deviation	2	6

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	290	290	
Age categorical Units: Subjects			
Adults (18-64 years)	156	156	
From 65-84 years	131	131	
85 years and over	3	3	
Age continuous Units: years			
arithmetic mean	62.6		
standard deviation	± 11.38	-	
Gender categorical Units: Subjects			
Female	172	172	
Male	118	118	
Race Units: Subjects			
Asian	13	13	
Black or African American	13	13	
White	244	244	
Other	20	20	

End points

End points reporting groups

Reporting group title	PerioChip
Reporting group description: 2.5 mg of chlorhexidine gluconate	
Reporting group title	Control
Reporting group description: Mechanical Subgingival Debridement	
Subject analysis set title	By-Pocket Analysis (PerioChip)
Subject analysis set type	Intention-to-treat
Subject analysis set description: By-pocket analysis of ITT population (PerioChip)	
Subject analysis set title	By-Pocket Analysis (Control)
Subject analysis set type	Intention-to-treat
Subject analysis set description: By-pocket analysis of ITT Population (Control)	
Subject analysis set title	Number of implants at Week 16 (PerioChip)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Number of implants at Week 16 in the ITT population (PerioChip)	
Subject analysis set title	Number of implants at Week 16 (Control)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Number of implants at Week 16 in the ITT population (Control)	
Subject analysis set title	Number of implants at Week 24 (PerioChip)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Number of implants at Week 24 in the ITT population (PerioChip)	
Subject analysis set title	Number of implants at Week 24 (Control)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Number of implants at Week 24 in the ITT population (Control)	

Primary: Mean Pocket Depth reduction (absolute change) for the selected target implant(s) at Week 24 compared to Baseline

End point title	Mean Pocket Depth reduction (absolute change) for the selected target implant(s) at Week 24 compared to Baseline
End point description:	
End point type	Primary
End point timeframe: Baseline to Week 24	

End point values	By-Pocket Analysis (PerioChip)	By-Pocket Analysis (Control)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	180	174		
Units: mm				
arithmetic mean (standard deviation)	-1.69 (± 1.18)	-1.51 (± 1.16)		

Statistical analyses

Statistical analysis title	Anaylsis of Primary Efficacy Endpoint
Comparison groups	By-Pocket Analysis (PerioChip) v By-Pocket Analysis (Control)
Number of subjects included in analysis	354
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	Mixed linear model

Secondary: Pocket Depth measurement at Week 16 compared to Baseline

End point title	Pocket Depth measurement at Week 16 compared to Baseline

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 16

End point values	By-Pocket Analysis (PerioChip)	By-Pocket Analysis (Control)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	179	166		
Units: mm				
arithmetic mean (standard deviation)	-1.36 (± 1.22)	-1.41 (± 1.12)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pocket Depth measurement at Week 24 compared to Baseline in patients with a Baseline PD measurement of 6 to 8 mm (inclusive)

End point title	Pocket Depth measurement at Week 24 compared to Baseline in patients with a Baseline PD measurement of 6 to 8 mm (inclusive)

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 24

End point values	PerioChip	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	141	130		
Units: mm				
arithmetic mean (standard deviation)	-1.77 (± 1.25)	-1.65 (± 1.18)		

Statistical analyses

No statistical analyses for this end point

Secondary: Bleeding on probing (BOP) measurements at Weeks 16 compared to Baseline

End point title	Bleeding on probing (BOP) measurements at Weeks 16 compared to Baseline

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 16

End point values	Number of implants at Week 16 (PerioChip)	Number of implants at Week 16 (Control)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	179	165		
Units: Number of patients				
BOP to BOP	96	82		
BOP to no BOP	76	73		
No BOP to BOP	3	2		
No BOP to no BOP	4	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Bleeding on probing (BOP) measurements at Week 24 compared to Baseline

End point title	Bleeding on probing (BOP) measurements at Week 24 compared to Baseline

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 24

End point values	Number of implants at Week 24 (PerioChip)	Number of implants at Week 24 (Control)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	180	173		
Units: Number of patients				
BOP to BOP	83	86		
BOP to no BOP	90	77		
No BOP to BOP	2	3		
No BOP to no BOP	5	7		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Baseline through Week 24	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0
Reporting groups	
Reporting group title	Safety
Reporting group description: -	

Serious adverse events	Safety		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 290 (2.41%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	2		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	1 / 290 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 290 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ventricular tachycardia			
subjects affected / exposed	1 / 290 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Facial paralysis			
subjects affected / exposed	1 / 290 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

General disorders and administration site conditions			
Death			
subjects affected / exposed	2 / 290 (0.69%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Musculoskeletal and connective tissue disorders			
Forearm fracture			
subjects affected / exposed	1 / 290 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Diverticulitis			
subjects affected / exposed	1 / 290 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Safety		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	68 / 290 (23.45%)		
Injury, poisoning and procedural complications			
Tooth repair			
subjects affected / exposed	5 / 290 (1.72%)		
occurrences (all)	8		
Aphthous ulcer			
subjects affected / exposed	4 / 290 (1.38%)		
occurrences (all)	6		
Artificial crown procedure			
subjects affected / exposed	3 / 290 (1.03%)		
occurrences (all)	3		
Tooth fracture			
subjects affected / exposed	3 / 290 (1.03%)		
occurrences (all)	4		
General disorders and administration			

site conditions			
Implant site pain			
subjects affected / exposed	12 / 290 (4.14%)		
occurrences (all)	16		
Post procedural discomfort			
subjects affected / exposed	6 / 290 (2.07%)		
occurrences (all)	8		
Gingivitis			
subjects affected / exposed	4 / 290 (1.38%)		
occurrences (all)	8		
Toothache			
subjects affected / exposed	4 / 290 (1.38%)		
occurrences (all)	5		
Gingival bleeding			
subjects affected / exposed	3 / 290 (1.03%)		
occurrences (all)	4		
Gingival pain			
subjects affected / exposed	3 / 290 (1.03%)		
occurrences (all)	3		
Headache			
subjects affected / exposed	3 / 290 (1.03%)		
occurrences (all)	3		
Hypersensitivity			
subjects affected / exposed	3 / 290 (1.03%)		
occurrences (all)	3		
Implant site swelling			
subjects affected / exposed	3 / 290 (1.03%)		
occurrences (all)	3		
Pharyngitis			
subjects affected / exposed	3 / 290 (1.03%)		
occurrences (all)	3		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	9 / 290 (3.10%)		
occurrences (all)	15		

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