

**Clinical trial results:****Effects of vitamin D supplementation during a non-surgical treatment of generalized chronic periodontitis: a randomized double-blinded placebo-controlled clinical trial****Summary**

EudraCT number	2016-005062-61
Trial protocol	BE
Global end of trial date	28 August 2019

Results information

Result version number	v1 (current)
This version publication date	17 February 2021
First version publication date	17 February 2021

Trial information**Trial identification**

Sponsor protocol code	Protocol01
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03162406
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cliniques universitaires Saint-Luc
Sponsor organisation address	Avenue Hippocrate, 10, Brussels, Belgium, 1200
Public contact	Ecole de Médecine Dentaire , Cliniques universitaires Saint-Luc, 32 27645702, jerome.lasserre@uclouvain.be
Scientific contact	Pr. Selena Toma, EMDS - Parodontologie, 32 27645714, selena.toma@uclouvain.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	28 August 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 August 2019
Global end of trial reached?	Yes
Global end of trial date	28 August 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The study wanted to test the hypothesis that vitamin D supplementation administered as an adjuvant to initial periodontal treatment and continued for 6 months in patients with generalized chronic periodontitis (GChP) and low serum vitamin D concentrations, may lead to superior clinical results compared with the initial treatment alone. The primary objective of this study was to determine the effect of vitamin D on probing pocket depth (PPD). The secondary objective was to validate the applied VD dosage regimen.

Protection of trial subjects:

The study was conducted in accordance with the guidelines of Good Clinical Practice and the revised Declaration of Helsinki for clinical studies

Background therapy:

Periodontitis is a chronic inflammatory disease characterized by immunoinflammatory infiltrate in the deep compartments of the periodontium, leading to destruction of the tooth-supporting tissues, tooth mobility and eventually tooth loss. In a recent systematic review on vitamin D levels and PD, Pinto et al. reported a significant association between low 25(OH)D levels and periodontal parameters in 65% of the cross-sectional studies analyzed. Still, among the observational longitudinal studies included, the authors found no proof that the PD progression could be attributed to lower serum 25(OH)D. Similar results were reported in another systematic review on vitamin D and PD. In both reviews, however, the authors could not identify the interventional studies where only vitamin D supplementation was used as adjuvant in the treatment of PD.

Therefore, there was a biologic rationale to investigate the anti-inflammatory effects of vitamin D supplementation during the treatment of periodontitis.

Evidence for comparator:

Vitamin D has been proposed to have anti-inflammatory properties that could be potentially appealing in the management of PD. The inflammation, when it is fine-tuned, is one of the principal defense mechanisms of the body. There is a controversy regarding the relationship between vitamin D and inflammation. If inflammatory conditions decrease 25(OH)D concentrations, and the body utilizes vitamin D to help heal and modulate inflammation, thus, obtaining higher vitamin D serum concentrations might be of benefit in treating these disorders. However, this hypothesis is not supported by some authors. In addition, analysis of cross-sectional data of the third National Health and Nutrition Examination Survey (NHANES III) found that the serum vitamin D levels were significantly and inversely associated with bleeding on gingival probing in all age groups, and Dietrich et al. reported a possible association between low serum vitamin D levels and PD.

Actual start date of recruitment	03 April 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 27
Worldwide total number of subjects	27
EEA total number of subjects	27

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)	27
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

30 years + older Caucasians (European + North African) in good general health and diagnosed with GChP based on the American Academy of Periodontology classification. They had to present a min 15 teeth (excluding 3d molars and teeth with advanced decay indicated for extraction). Serum 25(OH) vit D3 concentration for inclusion was set at <30 ng/mL

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	27
Intermediate milestone: Number of subjects	Enrollment: 27
Intermediate milestone: Number of subjects	Allocation: 27
Intermediate milestone: Number of subjects	Follow-up: 27
Intermediate milestone: Number of subjects	Analysis: 27
Number of subjects completed	27

Period 1

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

Blinding implementation details:

The principal examiner (M.P.) as well as the participants were blind to the respective treatment arms until the end of the study. Allocation concealment was warranted by the use of identical vitamin D/placebo ampoules produced by the company LABORATOIRES SMB S.A., Brussels, Belgium for the needs of the present study. After randomization, the two groups were followed in exactly the same way

Arms

Are arms mutually exclusive?	Yes
Arm title	VITAMIN D

Arm description:

25000 IU VITAMIN D WEEKLY per 6 months

Arm type	Experimental
Investigational medicinal product name	25000 IU VITAMIN D
Investigational medicinal product code	
Other name	VITAMIN D, D-CURE
Pharmaceutical forms	Solution for injection
Routes of administration	Oral use

Dosage and administration details:

25000 IU OF VITAMIN D PER WEEK FOR 6 MONTHS

Arm title	PLACEBO
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Arm description:

Ampoules produced by the company LABORATOIRES SMB S.A., Brussels, Belgium

Arm type	Placebo
Investigational medicinal product name	Ampoules produced by the company LABORATOIRES SMB S.A., Brussels, Belgium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Oral use

Dosage and administration details:

1 AMPOULE OF PLACEBO PER WEEK FOR 6 MONTHS

Number of subjects in period 1	VITAMIN D	PLACEBO
Started	13	14
Completed	13	14

Baseline characteristics

Reporting groups

Reporting group title	VITAMIN D
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Reporting group description:
25000 IU VITAMIN D WEEKLY per 6 months

Reporting group title	PLACEBO
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Reporting group description:
Ampoules produced by the company LABORATOIRES SMB S.A., Brussels, Belgium

Reporting group values	VITAMIN D	PLACEBO	Total
Number of subjects	13	14	27
Age categorical			
Patients with chronic periodontitis			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	13	14	27
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Patients with chronic periodontitis			
Units: years			
arithmetic mean	47.24	47.24	
standard deviation	± 8	± 8	-
Gender categorical			
Patients with chronic periodontitis			
Units: Subjects			
Female	3	4	7
Male	10	10	20
PPD			
Probing pocket depth			
Units: number			
arithmetic mean	67.70	49.64	
full range (min-max)	48.44 to 86.96	27.75 to 71.52	-

End points

End points reporting groups

Reporting group title	VITAMIN D
Reporting group description:	25000 IU VITAMIN D WEEKLY per 6 months
Reporting group title	PLACEBO
Reporting group description:	Ampoules produced by the company LABORATOIRES SMB S.A., Brussels, Belgium

Primary: Effect of vitamin D on non-surgical periodontal treatment

End point title	Effect of vitamin D on non-surgical periodontal treatment ^[1]
End point description:	The primary objective of this study was to determine the effect of vitamin D on probing pocket depth (PPD). The secondary objective was to validate the applied VD dosage regimen
End point type	Primary
End point timeframe:	The effect of vitamin d was evaluated at baseline - 3 months and 6 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 sample size was calculated by taking the PPD as the main measure with standard deviation of 0.5 mm to detect a difference of 1 mm. It took 7 subjects per group to have a power of 0.90 and 6 per group for a power of 0.80 (alpha = 0.05). To compensate for a possible dropout, an additional 20% of subjects were deemed necessary.

End point values	VITAMIN D	PLACEBO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	14		
Units: number				
arithmetic mean (full range (min-max))				
3 months	36.20 (22.47 to 49.93)	24.73 (12.19 to 37.26)		
6 months	24.80 (12.71 to 36.89)	20.45 (8.93 to 31.98)		

Statistical analyses

No statistical analyses for this end point

Secondary: Effect of vitamin D supplementation on FMPS and FMBS

End point title	Effect of vitamin D supplementation on FMPS and FMBS
End point description:	The secondary objectives of this study are to determine the effect of vitamin D supplementation on FMPS and FMBS
End point type	Secondary

End point timeframe:

The effect of vitamin D was evaluated at baseline - 3 months and 6 months

End point values	VITAMIN D	PLACEBO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	14		
Units: number				
arithmetic mean (standard deviation)				
FMPS - 3 months	0.28 (± 0.09)	0.25 (± 0.19)		
FMPS - 6 months	0.25 (± 0.17)	0.13 (± 0.11)		
FMBS - 3 months	0.19 (± 0.05)	0.18 (± 0.14)		
FMBS - 6 months	0.12 (± 0.07)	0.15 (± 0.11)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

April 2017-September 2018

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	10.0
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Reporting groups

Reporting group title	Test group
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Reporting group description:

vitamin D supplementation

Reporting group title	Control group
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Reporting group description:

placebo

Serious adverse events	Test group	Control group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Test group	Control group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)	

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: Zero non-serious adverse events

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