Clinical trial results:
A phase IV, randomised, cross-over study to estimate the influence of food on the 25-hydroxyvitamin D3 serum level after vitamin D3 (D-CURE®) supplementation.

Summary

EudraCT number	2014-003779-48
Trial protocol	BE
Global end of trial date	23 March 2015

Results information

Result version number	v1 (current)
This version publication date	12 February 2016
First version publication date	12 February 2016
Summary attachment (see zip file)	Synopsis (SMB D-CURE-IV-14-1 - CSR Synopsis V2.0_20151202.pdf)

Trial information

Trial identification

Sponsor protocol code	D-CURE-IV-14-1

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	LABORATOIRES SMB
Sponsor organisation address	26-28, rue de la Pastorale, 1082, Brussels, Belgium,
Public contact	CLINICAL DEPARTMENT, LABORATOIRES SMB S.A, 32 24120993, clinique@smb.be
Scientific contact	CLINICAL DEPARTMENT, LABORATOIRES SMB S.A, 32 24120993, clinique@smb.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	23 June 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 March 2015
Global end of trial reached?	Yes
Global end of trial date	23 March 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine whether administration of vitamin D3 (D-CURE®) with food will improve the absorption and increase serum levels of 25-hydroxyvitamin D3.

Protection of trial subjects:

For this study, no specific measures were put in place to protect trial subjects. The study treatment D-CURE was a product marketed by the Laboratoires SMB since 1974 in Belgium and then was well known by most of the participating subjects.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 October 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	Belgium: 88
Worldwide total number of subjects	88
EEA total number of subjects	88

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)	88
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted in one center in Belgium. The subject recruitment was adequate to meet the target enrolment goal of 88 subjects in less than one month (22/10/2014 - 06/11/2014). After the screening visit, the subjects were randomized in one of the two sequences of treatment. The study extended over two periods of 60+-3 days.

Pre-assignment

Screening details:

-Obtain signed ICF
-Obtain demographic data
-Perform a medical history & physical examination
-Take vital signs
-Review prior/concomitant medications
-Perform a 25(OH)-D serum concentration assessment and laboratory evaluations : haematology, chemistry, calcium, phosphate, TSH, blood pregnancy test
-Review inclusion/exclusion criteria

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	D-CURE with standardized high fat breakfast

Arm description:

The subjects received 2 ampoules of D-CURE of 25.000 IU (total = 50.000 IU) on the first day of the period with a standardized high fat breakfast and stayed at the study site during 4 hours after the drug administration.

Arm type	Experimental
Investigational medicinal product name	D-CURE 1 ml ampoule containing 25.000 IU
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Two ampoules of D-CURE (total 50.000 IU) were taken at the beginning of each of the two study periods in either fasting condition or after a standardized high fat breakfast according to the randomization list.

Arm title	D-CURE in fasting condition

Arm description:

The subjects received 2 ampoules of D-CURE of 25.000 IU (total = 50.000 IU) on the first day of the period in fasting conditions and stayed at the study site during 4 hours after the drug administration.

Arm type	Experimental
Investigational medicinal product name	D-CURE 1 ml ampoule containing 25.000 IU
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Two ampoules of D-CURE (total 50.000 IU) were taken at the beginning of each of the two study periods in either fasting condition or after a standardized high fat breakfast according to the randomization list.

Number of subjects in period 1	D-CURE with standardized high fat breakfast	D-CURE in fasting condition
Started	88	88
Completed	88	88

Baseline characteristics

Reporting groups	
Reporting group title	Cross over phase

Reporting group description:

After being screened, 88 subjects were randomized in this study and completed the study.
No premature withdrawal of randomized subjects was observed in the study.
The safety and the ITT analysis were then performed on 88 patients.

Reporting group values	Cross over phase	Total	
Number of subjects	88	88	
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)	88	88	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	31.3		
standard deviation	± 8.8	-	
Gender categorical Units: Subjects			
Female	51	51	
Male	37	37	

End points

End points reporting groups

Reporting group title	D-CURE with standardized high fat breakfast
Reporting group description:	
The subjects received 2 ampoules of D-CURE of 25.000 IU (total = 50.000 IU) on the first day of the period with a standardized high fat breakfast and stayed at the study site during 4 hours after the drug administration.	
Reporting group title	D-CURE in fasting condition
Reporting group description:	
The subjects received 2 ampoules of D-CURE of 25.000 IU (total = 50.000 IU) on the first day of the period in fasting conditions and stayed at the study site during 4 hours after the drug administration.	

Primary: Mean change in serum 25(OH)D3 levels from baseline to D14.

End point title	Mean change in serum 25(OH)D3 levels from baseline to D14.
End point description:	
End point type	Primary
End point timeframe:	
baseline and Day 14 of each period.	

End point values	D-CURE with standardized high fat breakfast	D-CURE in fasting condition		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	88		
Units: ng/ml				
arithmetic mean (standard deviation)	9.1 (± 4.1)	8.5 (± 3.8)		

Statistical analyses

Statistical analysis title	Mixed model
Comparison groups	D-CURE with standardized high fat breakfast v D-CURE in fasting condition
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.025
Method	t-test, 1-sided
Parameter estimate	Mean difference (final values)

Confidence interval	
level	Other: 97.5 %
sides	1-sided
lower limit	-0.2
Variability estimate	Standard error of the mean

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The AEs were recorded during the entire study period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18

Reporting groups

Reporting group title	D-CURE with standardized high fat breakfast

Reporting group description:

The subjects received 2 ampoules of D-CURE of 25.000 IU (total = 50.000 IU) on the first day of the period with a standardized high fat breakfast and stayed at the study site during 4 hours after the drug administration.

Reporting group title	D-CURE in fasting condition

Reporting group description:

The subjects received 2 ampoules of D-CURE of 25.000 IU (total = 50.000 IU) on the first day of the period in fasting conditions and stayed at the study site during 4 hours after the drug administration.

Serious adverse events	D-CURE with standardized high fat breakfast	D-CURE in fasting condition	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 88 (0.00%)	0 / 88 (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: 5 %

Non-serious adverse events	D-CURE with standardized high fat breakfast	D-CURE in fasting condition	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 88 (6.82%)	7 / 88 (7.95%)	
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 88 (6.82%)	7 / 88 (7.95%)	
occurrences (all)	8	8	

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