Clinical trial results:
A phase IV, two-armed, randomised, cross-over study to compare the compliance of a once-a-month administration of vitamin D3 (D-CURE®) to a daily administration of a fixed-dose combination of vitamin D3 and calcium (STEOVIT FORTE®) during two periods of 6 months.

Summary

EudraCT number	2012-003417-34
Trial protocol	BE
Global end of trial date	17 February 2014

Results information

Result version number	v1 (current)
This version publication date	23 February 2016
First version publication date	01 March 2015
Summary attachment (see zip file)	C-CURE IV-12-1 CSR synopsis (D-CURE IV-12-1 - Clinical Report synopsis version 1.0.pdf)

Trial information

Trial identification

Sponsor protocol code	D-CURE-IV-12-1

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	rue de la Pastorale, Brussels, Belgium,
Public contact	CLINICAL DEPARTMENT, LABORATOIRES SMB S.A., 32 2 412 09 93, clinique@smb.be
Scientific contact	CLINICAL DEPARTMENT, LABORATOIRES SMB S.A., 32 2 412 09 93, 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	06 June 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 February 2014
Global end of trial reached?	Yes
Global end of trial date	17 February 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of the present study is to assess the compliance of a once-a-month administration of vitamin D3 (D-CURE®) to a daily administration of a fixed-dose combination of vitamin D3 and calcium (STEOVIT FORTE®) during two periods of 6 months and to see their effect on the level of vitamin D.

Protection of trial subjects:

No particular protection of trial subjects were taken.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 October 2012
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: 100
Worldwide total number of subjects	100
EEA total number of subjects	100

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)	37
From 65 to 84 years	60
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

After being screened for the study, volunteers were randomised in the study for two periods of 6 months during which they received each treatment according to the randomisation scheme.

Pre-assignment

Screening details:

Eligible volunteers were over 50 years old and gave their informed consent.

Period 1

Period 1 title	Period 1 - first 6-month treatment
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Study not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	D-CURE

Arm description: -

Arm type	Experimental
Investigational medicinal product name	vitamin D3
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

One ampoule of D-CURE® 25.000 IU will be taken, orally, once a month, during 6 months.

Arm title	STEOVIT FORTE

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	vitamin D3/calcium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

One tablet of STEOVIT FORTE® 800 IU/1g will be taken, orally, once a day, during 6 months.

Number of subjects in period 1	D-CURE	STEOVIT FORTE
Started	50	50
After the first 6-month treatment period	50	49
Completed	50	49
Not completed	0	1

Consent withdrawn by subject	-	1

Period 2	
Period 2 title	Period 2 - the second 6-month treatment
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	Yes
Arm title	D-CURE
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	vitamin D3
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

One ampoule of D-CURE® 25.000 IU will be taken, orally, once a month, during 6 months.

Arm title	STEOVIT FORTE
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	vitamin D3/calcium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

One tablet of STEOVIT FORTE® 800 IU/1g will be taken, orally, once a day, during 6 months.

Number of subjects in period 2	D-CURE	STEOVIT FORTE
Started	50	49
After the second6-month treatment	48	43
Completed	48	43
Not completed	2	6
Patient moved to Luxembourg	1	-
Adverse event, serious fatal	-	1

Consent withdrawn by subject	1	1
Adverse event, non-fatal	-	3
Lost to follow-up	-	1

Baseline characteristics

Reporting groups	
Reporting group title	D-CURE
Reporting group description: -	
Reporting group title	STEOVIT FORTE
Reporting group description: -	

Reporting group values	D-CURE	STEOVIT FORTE	Total
Number of subjects	50	50	100
Age categorical 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)	18	19	37
From 65-84 years	30	30	60
85 years and over	2	1	3
Age continuous Units: years			
median	65.5	67.5	
inter-quartile range (Q1-Q3)	57.4 to 72.7	61.2 to 73.8	-
Gender categorical Units: Subjects			
Female	14	13	27
Male	36	37	73

End points

End points reporting groups	
Reporting group title	D-CURE
Reporting group description: -	
Reporting group title	STEOVIT FORTE
Reporting group description: -	
Reporting group title	D-CURE
Reporting group description: -	
Reporting group title	STEOVIT FORTE
Reporting group description: -	

Primary: Compliance over 6-month treatments periods	
End point title	Compliance over 6-month treatments periods
End point description:	
End point type	Primary
End point timeframe:	
Calculated after each 6-month treatment periods	

End point values	D-CURE	STEOVIT FORTE	D-CURE	STEOVIT FORTE
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	49	50	49
Units: percentage	100	88	106	82

Statistical analyses

Statistical analysis title	Two sample t-test
Comparison groups	D-CURE v STEOVIT FORTE
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Variability estimate	Standard deviation

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The adverse events were collected by the investigator during the course of the study (at each study visit).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	D-CURE

Reporting group description:

D-CURE® 1 ml ampoule containing 25 000 IU/ml of cholecalciferol taken orally once a month.

Reporting group title	Steovit Forte

Reporting group description:

STEOVIT FORTE® tablet containing 1000 mg of calcium and 800 IU of cholecalciferol taken orally once a day.

Serious adverse events	D-CURE	Steovit Forte	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 99 (6.06%)	6 / 99 (6.06%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Intestinal adenocarcinoma			
subjects affected / exposed	0 / 99 (0.00%)	1 / 99 (1.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	0 / 99 (0.00%)	1 / 99 (1.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Breast cancer			
subjects affected / exposed	1 / 99 (1.01%)	0 / 99 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			

subjects affected / exposed	1 / 99 (1.01%)	0 / 99 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	1 / 99 (1.01%)	0 / 99 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Hernia repair			
subjects affected / exposed	1 / 99 (1.01%)	0 / 99 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract operation			
subjects affected / exposed	1 / 99 (1.01%)	0 / 99 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 99 (1.01%)	0 / 99 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	1 / 99 (1.01%)	0 / 99 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 99 (0.00%)	1 / 99 (1.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Joint prosthesis user			

subjects affected / exposed	0 / 99 (0.00%)	1 / 99 (1.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 99 (0.00%)	1 / 99 (1.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess			
subjects affected / exposed	0 / 99 (0.00%)	1 / 99 (1.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	1 / 99 (1.01%)	0 / 99 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	D-CURE	Steovit Forte	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 99 (12.12%)	17 / 99 (17.17%)	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	4 / 99 (4.04%)	5 / 99 (5.05%)	
occurrences (all)	4	5	
Nausea			
subjects affected / exposed	1 / 99 (1.01%)	5 / 99 (5.05%)	
occurrences (all)	1	5	
Infections and infestations			
Bronchitis			
subjects affected / exposed	7 / 99 (7.07%)	7 / 99 (7.07%)	
occurrences (all)	7	10	

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