Clinical trial results:
Comparative study of the effect of 4-week treatment with ossein-hydroxyapatite compound versus calcium carbonate on bone biomarkers in young women with low calcium intake. Prospective, monocenter, randomized, open-label, two-period,cross-over trial

Summary

EudraCT number	2008-002280-14
Trial protocol	FR
Global end of trial date	13 January 2009

Results information

Result version number	v1 (current)
This version publication date	28 December 2018
First version publication date	28 December 2018

Trial information

Trial identification

Sponsor protocol code	L00006 CP 403 3A

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Pierre Fabre Médicament
Sponsor organisation address	45 place Abel Gance, Boulogne, France, 92654
Public contact	Dr Mohammed ZAÏM, Institut de Recherche Pierre Fabre (IRPF), +33 (0)5-34-50-61-91, mohammed.zaim@pierre-fabre.com
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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	13 January 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 January 2009
Global end of trial reached?	Yes
Global end of trial date	13 January 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study is to compare the effect of 4-week treatment with ossein-hydroxyapatite compound versus calcium carbonate on biochemical markers of bone resorption in young women with low calcium intake.

Protection of trial subjects:

The study was conducted according to Good Clinical Practice (GCP) (CPMP/ICH/135/95), the principles stated in the Declaration of Helsinki (1964) and its subsequent amendments thereto, and national regulations. The request for authorization by the Competent Authority or its notification (depending on National Regulations) was carried out by the Sponsor. The study protocol and related documents, including the informed consent forms (ICFs), were submitted for approval to independent, local or national Independent Ethics Committees (IECs) and to competent authorities (CAs) before the study set-up, according to national regulations.

Background therapy:

No specific therapy was given during the study

Evidence for comparator:

Calcium carbonate is considered to be a well bioavailable form of oral calcium. For the main efficacy criteria (biomarkers of resorption), a wash-out period of 4 weeks is considered sufficient to bring the values noted after the first treatment period back to baseline and thus avoid or minimise any possible carry-over effect.

Actual start date of recruitment	09 September 2008
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	France: 58
Worldwide total number of subjects	58
EEA total number of subjects	58

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	58
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 72 subjects were offered enrolment in the study. Of them, 12 were not randomised and 60 were effectively included and randomised. Premature withdrawal from therapy occurred in 2 subjects (not inculded in the FAS).

Pre-assignment

Screening details:

72 young women with low calcium intake were offered enrolment. Low calcium intake is more frequent in young women than men. Moreover, osteoporosis is more prevalent amongst females than males.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Osteopor-Orocal

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Osteopor
Investigational medicinal product code	
Other name	Ossein-hydroxyapatite, L0006
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Two tablets of 830 mg to be swallowed with a glass of tap water, twice daily in the morning and evening before meals for four weeks.

Arm title	Orocal-Osteopor

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Orocal
Investigational medicinal product code	
Other name	Calcium carbonate
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One tablet to be sucked twice daily in the morning and evening before meals for four weeks.

Number of subjects in period 1	Osteopor-Orocal	Orocal-Osteopor
Started	29	29
Completed	29	29

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Osteopor-Orocal

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Orocal
Investigational medicinal product code	
Other name	Calcium carbonate
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One tablet to be sucked twice daily in the morning and evening before meals for four weeks.

Arm title	Orocal-Osteopor

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Osteopor
Investigational medicinal product code	
Other name	Ossein-hydroxyapatite, L0006
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Two tablets of 830 mg to be swallowed with a glass of tap water, twice daily in the morning and evening before meals for four weeks.

Number of subjects in period 2	Osteopor-Orocal	Orocal-Osteopor
Started	29	29
Completed	29	29

Baseline characteristics

Reporting groups	
Reporting group title	Osteopor-Orocal
Reporting group description: -	
Reporting group title	Orocal-Osteopor
Reporting group description: -	

Reporting group values	Osteopor-Orocal	Orocal-Osteopor	Total
Number of subjects	29	29	58
Age categorical Units: Subjects			
Adults (18-64 years)	29	29	58
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	22.6	21.7	
standard deviation	± 2.4	± 2.2	-
Gender categorical Units: Subjects			
Female	29	29	58
Male	0	0	0
Height Units: cm			
arithmetic mean	166.1	164.0	
standard deviation	± 7.8	± 4.7	-
Weight Units: kg			
arithmetic mean	57.31	57.51	
standard deviation	± 7.68	± 5.26	-
Body Mass Index derived Units: kg/m²			
arithmetic mean	20.72	21.40	
standard deviation	± 1.91	± 2.01	-

End points

End points reporting groups	
Reporting group title	Osteopor-Orocal
Reporting group description: -	
Reporting group title	Orocal-Osteopor
Reporting group description: -	
Reporting group title	Osteopor-Orocal
Reporting group description: -	
Reporting group title	Orocal-Osteopor
Reporting group description: -	

Primary: Serum type-I collagen cross-linked C-telopeptide (CTX1)	
End point title	Serum type-I collagen cross-linked C-telopeptide (CTX1)
End point description:	
End point type	Primary
End point timeframe:	
The study main efficacy criterion was the change from baseline in serum concentration of the bone resorption biomarker CTX1 after 4 weeks of treatment.	

End point values	Osteopor-Orocal	Orocal-Osteopor	Osteopor-Orocal	Orocal-Osteopor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	29	29	29
Units: pmol/L				
arithmetic mean (standard deviation)				
Start	4872.8 (± 2182.1)	4714.1 (± 2260.3)	5168.7 (± 1866.7)	4812.8 (± 2284.8)
End	4642.3 (± 1406.3)	3961.6 (± 2231.9)	4827.7 (± 1600.3)	4437.5 (± 1833.7)

Statistical analyses

Statistical analysis title	Full analysis set
Comparison groups	Osteopor-Orocal v Orocal-Osteopor
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.36
Method	Test of the three effects of interest

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from subject's inclusion to the end of study. Any SAE occurring during the month following the last administration of the study drug or the
end of the study was to be notified to the Sponsor.

Adverse event reporting additional description:

Any disease existing at subjects' selection was reported in the CRF. At each further visit (or phone call), the occurrence of AEs since the last visit was collected on the basis of subject's spontaneous reporting, Investigator's non-leading questioning and/or clinical assessments.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Osteopor-Orocal
Reporting group description: -	
Reporting group title	Orocal-Osteopor

Reporting group description: -

Serious adverse events	Osteopor-Orocal	Orocal-Osteopor	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (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: 3.3 %

Non-serious adverse events	Osteopor-Orocal	Orocal-Osteopor	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 29 (62.07%)	12 / 29 (41.38%)	
Surgical and medical procedures			
Dental operation			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Nervous system disorders			
vasovagal syncope			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Gastrointestinal disorders			

Constipation			
subjects affected / exposed	2 / 29 (6.90%)	2 / 29 (6.90%)	
occurrences (all)	2	2	
Dry mouth			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Teething			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Choking			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 29 (3.45%)	2 / 29 (6.90%)	
occurrences (all)	1	2	
Bronchitis			
subjects affected / exposed	2 / 29 (6.90%)	2 / 29 (6.90%)	
occurrences (all)	2	2	
Acute tonsillitis			
subjects affected / exposed	4 / 29 (13.79%)	0 / 29 (0.00%)	
occurrences (all)	4	0	
Gastroenteritis			
subjects affected / exposed	4 / 29 (13.79%)	2 / 29 (6.90%)	
occurrences (all)	4	2	
Influenza			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences (all)	1	0	

Sinusitis subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	0 / 29 (0.00%) 0	
Tooth abscess subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	0 / 29 (0.00%) 0	

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