Clinical trial results:
A Randomized, Open-Label, 2-Way Cross-over, Phase 4 Study to Evaluate Subject Preference and Acceptability of a New Formulation of Calcichew D3 in Adult Patients Eligible for Calcium and Vitamin D Supplementation.

Summary

EudraCT number	2014-005619-18
Trial protocol	GB DE
Global end of trial date	27 August 2015

Results information

Result version number	v1
This version publication date	18 June 2016
First version publication date	18 June 2016

Trial information

Trial identification

Sponsor protocol code	Calcichew-4001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02457247
WHO universal trial number (UTN)	U1111-1166-8818
Other trial identifiers	15/NW/0275: NRES

Notes:

Sponsors

Sponsor organisation name	Takeda Development Center Americas, Inc.
Sponsor organisation address	One Takeda Parkway, Deerfield, United States, 60015
Public contact	Takeda, Medical Director, Clinical Science, +1 877-825-3327, clinicaltrialregistry@tpna.com
Scientific contact	Takeda, Medical Director, Clinical Science, +1 877-825-3327, clinicaltrialregistry@tpna.com

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	27 August 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 August 2015
Global end of trial reached?	Yes
Global end of trial date	27 August 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to compare the preference of Calcichew D3 500/400 (containing 500 mg calcium and 400 IU of vitamin D) with Adcal-D3 600/400 (containing 600 mg of calcium and 400 IU of vitamin D) in Test Group 1, and to compare Calcichew D3 500/800 (containing 500 mg calcium and 800 IU vitamin D) with Kalcipos-D 500/800 (containing 500 mg of calcium and 800 IU of vitamin D) in Test Group 2.

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 June 2015
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: 138
Country: Number of subjects enrolled	Germany: 138
Worldwide total number of subjects	276
EEA total number of subjects	276

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)	19
From 65 to 84 years	254
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 9 investigative sites in the United Kingdom and Germany from 02 June 2015 to 27 August 2015.

Pre-assignment

Screening details:

Participants eligible for Vitamin D and Calcium supplements were enrolled equally in 1 of 2 Test Groups to determine the preference between 2 treatments.
Group 1: Calcichew D3 500/400 and Adcal-D3 600/400 or Group 2: Calcichew D3 500/800 and Kalcipos-D 500/800.

Period 1

Period 1 title	Period 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Test Group 1: Sequence AB

Arm description:

Calcichew D3 500/400 (Calcium 500 mg/400 IU Vitamin D3) [A], chewable tablets, orally, twice, daily, on Days 1 through 14, followed by Adcal-D3 (Calcium 600 mg / 400 IU Vitamin D3) [B], chewable tablets, orally, twice, daily, on Days 15 through 28.

Arm type	Experimental
Investigational medicinal product name	Calcichew D3
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

Calcichew D3 500/400 (Calcium 500 mg/400 IU Vitamin D3), chewable tablets, orally, twice, daily.

Investigational medicinal product name	Adcal-D3
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

Adcal-D3 (Calcium 600 mg / 400 IU Vitamin D3), chewable tablets, orally, twice, daily.

Arm title	Test Group 1: Sequence BA

Arm description:

Adcal-D3 (Calcium 600 mg / 400 IU Vitamin D3), chewable tablets, orally, twice, daily, on Days 1 through 14, followed by, Calcichew D3 500/400 (Calcium 500 mg/400 IU Vitamin D3), chewable tablets, orally, twice, daily, on Days 15 through 28.

Arm type	Experimental

Investigational medicinal product name	Calcichew D3
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

Calcichew D3 500/400 (Calcium 500 mg/400 IU Vitamin D3), chewable tablets, orally, twice, daily.

Investigational medicinal product name	Adcal-D3
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

Adcal-D3 (Calcium 600 mg / 400 IU Vitamin D3), chewable tablets, orally, twice, daily.

Arm title	Test Group 2: Sequence CD

Arm description:

Calcichew D3 500/800 (Calcium 500 mg/800 IU Vitamin D3) [C], chewable tablets, orally, once, daily, on Days 1 through 14, followed by Kalcipos-D (Calcium 500 mg/800 IU Vitamin D3) [D], chewable tablets, orally, once, daily, on Days 15 through 28.

Arm type	Experimental
Investigational medicinal product name	Calcichew D3
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

Calcichew D3 500/400 (Calcium 500 mg/400 IU Vitamin D3), chewable tablets, orally, twice, daily.

Investigational medicinal product name	Kalcipos-D
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

Kalcipos-D (Calcium 500 mg/800 IU Vitamin D3), chewable tablets, orally, once, daily.

Arm title	Test Group 2: Sequence DC

Arm description:

Kalcipos-D (Calcium 500 mg/800 IU Vitamin D3), chewable tablets, orally, once, daily, on Days 1 through 14, followed by, Calcichew D3 500/800 (Calcium 500 mg/800 IU Vitamin D3), chewable tablets, orally, once, daily, on Days 15 through 28.

Arm type	Experimental
Investigational medicinal product name	Kalcipos-D
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

Kalcipos-D (Calcium 500 mg/800 IU Vitamin D3), chewable tablets, orally, once, daily.

Investigational medicinal product name	Calcichew D3
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

Calcichew D3 500/400 (Calcium 500 mg/400 IU Vitamin D3), chewable tablets, orally, twice, daily.

Number of subjects in period 1	Test Group 1: Sequence AB	Test Group 1: Sequence BA	Test Group 2: Sequence CD
Started	68	70	68
Completed	66	68	68
Not completed	2	2	0
Pretreatment Event/Adverse Event	-	1	-
Voluntary Withdrawal	1	-	-
Significant Protocol Deviation	1	1	-

Number of subjects in period 1	Test Group 2: Sequence DC
Started	70
Completed	70
Not completed	0
Pretreatment Event/Adverse Event	-
Voluntary Withdrawal	-
Significant Protocol Deviation	-

Period 2

Period 2 title	Period 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Test Group 1: Sequence AB

Arm description:

Calcichew D3 500/400 (Calcium 500 mg/400 IU Vitamin D3) [A], chewable tablets, orally, twice, daily, on Days 1 through 14, followed by Adcal-D3 (Calcium 600 mg / 400 IU Vitamin D3) [B], chewable tablets, orally, twice, daily, on Days 15 through 28.

Arm type	Experimental

Investigational medicinal product name	Calcichew D3
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

Calcichew D3 500/400 (Calcium 500 mg/400 IU Vitamin D3), chewable tablets, orally, twice, daily.

Investigational medicinal product name	Adcal-D3
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

Adcal-D3 (Calcium 600 mg / 400 IU Vitamin D3), chewable tablets, orally, twice, daily.

Arm title	Test Group 1: Sequence BA

Arm description:

Adcal-D3 (Calcium 600 mg / 400 IU Vitamin D3), chewable tablets, orally, twice, daily, on Days 1 through 14, followed by, Calcichew D3 500/400 (Calcium 500 mg/400 IU Vitamin D3), chewable tablets, orally, twice, daily, on Days 15 through 28.

Arm type	Experimental
Investigational medicinal product name	Calcichew D3
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

Calcichew D3 500/400 (Calcium 500 mg/400 IU Vitamin D3), chewable tablets, orally, twice, daily.

Investigational medicinal product name	Adcal-D3
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

Adcal-D3 (Calcium 600 mg / 400 IU Vitamin D3), chewable tablets, orally, twice, daily.

Arm title	Test Group 2: Sequence CD

Arm description:

Calcichew D3 500/800 (Calcium 500 mg/800 IU Vitamin D3) [C], chewable tablets, orally, once, daily, on Days 1 through 14, followed by Kalcipos-D (Calcium 500 mg/800 IU Vitamin D3) [D], chewable tablets, orally, once, daily, on Days 15 through 28.

Arm type	Experimental
Investigational medicinal product name	Calcichew D3
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

Calcichew D3 500/400 (Calcium 500 mg/400 IU Vitamin D3), chewable tablets, orally, twice, daily.

Investigational medicinal product name	Kalcipos-D
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

Kalcipos-D (Calcium 500 mg/800 IU Vitamin D3), chewable tablets, orally, once, daily.

Arm title	Test Group 2: Sequence DC

Arm description:

Kalcipos-D (Calcium 500 mg/800 IU Vitamin D3), chewable tablets, orally, once, daily, on Days 1 through 14, followed by, Calcichew D3 500/800 (Calcium 500 mg/800 IU Vitamin D3), chewable tablets, orally, once, daily, on Days 15 through 28.

Arm type	Experimental
Investigational medicinal product name	Kalcipos-D
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

Kalcipos-D (Calcium 500 mg/800 IU Vitamin D3), chewable tablets, orally, once, daily.

Investigational medicinal product name	Calcichew D3
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

Calcichew D3 500/400 (Calcium 500 mg/400 IU Vitamin D3), chewable tablets, orally, twice, daily.

Number of subjects in period 2	Test Group 1: Sequence AB	Test Group 1: Sequence BA	Test Group 2: Sequence CD
Started	66	68	68
Completed	64	65	68
Not completed	2	3	0
Pretreatment Event/Adverse Event	-	1	-
Voluntary Withdrawal	1	1	-
Significant Protocol Deviation	1	-	-
Lost to follow-up	-	1	-

Number of subjects in period 2	Test Group 2: Sequence DC
Started	70
Completed	70
Not completed	0
Pretreatment Event/Adverse Event	-
Voluntary Withdrawal	-
Significant Protocol Deviation	-
Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	Test Group 1: Sequence AB
Reporting group description:	
Calcichew D3 500/400 (Calcium 500 mg/400 IU Vitamin D3) [A], chewable tablets, orally, twice, daily, on Days 1 through 14, followed by Adcal-D3 (Calcium 600 mg / 400 IU Vitamin D3) [B], chewable tablets, orally, twice, daily, on Days 15 through 28.	
Reporting group title	Test Group 1: Sequence BA
Reporting group description:	
Adcal-D3 (Calcium 600 mg / 400 IU Vitamin D3), chewable tablets, orally, twice, daily, on Days 1 through 14, followed by, Calcichew D3 500/400 (Calcium 500 mg/400 IU Vitamin D3), chewable tablets, orally, twice, daily, on Days 15 through 28.	
Reporting group title	Test Group 2: Sequence CD
Reporting group description:	
Calcichew D3 500/800 (Calcium 500 mg/800 IU Vitamin D3) [C], chewable tablets, orally, once, daily, on Days 1 through 14, followed by Kalcipos-D (Calcium 500 mg/800 IU Vitamin D3) [D], chewable tablets, orally, once, daily, on Days 15 through 28.	
Reporting group title	Test Group 2: Sequence DC
Reporting group description:	
Kalcipos-D (Calcium 500 mg/800 IU Vitamin D3), chewable tablets, orally, once, daily, on Days 1 through 14, followed by, Calcichew D3 500/800 (Calcium 500 mg/800 IU Vitamin D3), chewable tablets, orally, once, daily, on Days 15 through 28.	

Reporting group values	Test Group 1: Sequence AB	Test Group 1: Sequence BA	Test Group 2: Sequence CD
Number of subjects	68	70	68
Age categorical			
Units: Subjects			
Adults (18-64 years)	0	0	8
From 65-84 years	68	69	58
85 years and over	0	1	2
Age continuous			
Units: years			
arithmetic mean	70.9	70.8	70.9
standard deviation	± 7.37	± 4.94	± 7.37
Gender categorical			
Units: Subjects			
Female	40	41	60
Male	28	29	8
Race/Ethnicity, Customized			
Units: Subjects			
Asian	1	3	0
Multiracial	0	1	0
White	67	66	68
BMI Categorical			
Units: Subjects			
<25 kg/m^2	11	17	30
25 to <30 kg/m^2	30	29	27
≥30 kg/m^2	24	24	11
Missing	3	0	0
Smoking Status			

Units: Subjects			
Never Smoked	28	31	41
Ex-smoker	32	33	18
Current Smoker	8	6	9
Alcohol Status Units: Subjects			
Never Drank	11	14	10
Ex-drinker	4	10	5
Current Drinker	53	46	53
History of Osteoporosis Units: Subjects			
Yes	1	3	28
No	67	67	40
History of Fractures in the Last 10 Years Units: Subjects			
Yes	11	10	7
No	57	60	61
Region of Enrollment Units: Subjects			
United Kingdom	68	70	0
Germany	0	0	68
History of Osteopenia Units: Subjects			
Yes	7	3	7
No	61	67	61
Height			
Height data is available for 65, 70, 68 and 70 participants, respectively.			
Units: cm			
arithmetic mean	164.4	165.4	164
standard deviation	± 7.44	± 8.95	± 7.73
Weight Units: kg			
arithmetic mean	78.92	81.72	71.44
standard deviation	± 15.383	± 23.559	± 13.799
Body Mass Index (BMI)			
BMI data is available for 65, 70, 68 and 70 participants, respectively.			
Units: kg/m^2			
arithmetic mean	29.157	29.588	26.478
standard deviation	± 4.7766	± 6.571	± 4.2362

Reporting group values	Test Group 2: Sequence DC	Total	
Number of subjects	70	276	
Age categorical Units: Subjects			
Adults (18-64 years)	11	19	
From 65-84 years	59	254	
85 years and over	0	3	
Age continuous Units: years			
arithmetic mean	69.9		
standard deviation	± 7.03	-	

Gender categorical Units: Subjects			
Female	60	201	
Male	10	75	
Race/Ethnicity, Customized Units: Subjects			
Asian	1	5	
Multiracial	0	1	
White	69	270	
BMI Categorical Units: Subjects			
<25 kg/m^2	27	85	
25 to <30 kg/m^2	27	113	
≥30 kg/m^2	16	75	
Missing	0	3	
Smoking Status Units: Subjects			
Never Smoked	35	135	
Ex-smoker	24	107	
Current Smoker	11	34	
Alcohol Status Units: Subjects			
Never Drank	12	47	
Ex-drinker	2	21	
Current Drinker	56	208	
History of Osteoporosis Units: Subjects			
Yes	24	56	
No	46	220	
History of Fractures in the Last 10 Years Units: Subjects			
Yes	8	36	
No	62	240	
Region of Enrollment Units: Subjects			
United Kingdom	0	138	
Germany	70	138	
History of Osteopenia Units: Subjects			
Yes	12	29	
No	58	247	
Height			
Height data is available for 65, 70, 68 and 70 participants, respectively.			
Units: cm			
arithmetic mean	164.8		
standard deviation	± 7.78	-	
Weight Units: kg			
arithmetic mean	73.61		
standard deviation	± 16.34	-	
Body Mass Index (BMI)			

BMI data is available for 65, 70, 68 and 70 participants, respectively.			
Units: kg/m^2			
arithmetic mean	27.002		
standard deviation	± 5.1081	-	

End points

End points reporting groups

Reporting group title	Test Group 1: Sequence AB
Reporting group description:	
Calcichew D3 500/400 (Calcium 500 mg/400 IU Vitamin D3) [A], chewable tablets, orally, twice, daily, on Days 1 through 14, followed by Adcal-D3 (Calcium 600 mg / 400 IU Vitamin D3) [B], chewable tablets, orally, twice, daily, on Days 15 through 28.	
Reporting group title	Test Group 1: Sequence BA
Reporting group description:	
Adcal-D3 (Calcium 600 mg / 400 IU Vitamin D3), chewable tablets, orally, twice, daily, on Days 1 through 14, followed by, Calcichew D3 500/400 (Calcium 500 mg/400 IU Vitamin D3), chewable tablets, orally, twice, daily, on Days 15 through 28.	
Reporting group title	Test Group 2: Sequence CD
Reporting group description:	
Calcichew D3 500/800 (Calcium 500 mg/800 IU Vitamin D3) [C], chewable tablets, orally, once, daily, on Days 1 through 14, followed by Kalcipos-D (Calcium 500 mg/800 IU Vitamin D3) [D], chewable tablets, orally, once, daily, on Days 15 through 28.	
Reporting group title	Test Group 2: Sequence DC
Reporting group description:	
Kalcipos-D (Calcium 500 mg/800 IU Vitamin D3), chewable tablets, orally, once, daily, on Days 1 through 14, followed by, Calcichew D3 500/800 (Calcium 500 mg/800 IU Vitamin D3), chewable tablets, orally, once, daily, on Days 15 through 28.	
Reporting group title	Test Group 1: Sequence AB
Reporting group description:	
Calcichew D3 500/400 (Calcium 500 mg/400 IU Vitamin D3) [A], chewable tablets, orally, twice, daily, on Days 1 through 14, followed by Adcal-D3 (Calcium 600 mg / 400 IU Vitamin D3) [B], chewable tablets, orally, twice, daily, on Days 15 through 28.	
Reporting group title	Test Group 1: Sequence BA
Reporting group description:	
Adcal-D3 (Calcium 600 mg / 400 IU Vitamin D3), chewable tablets, orally, twice, daily, on Days 1 through 14, followed by, Calcichew D3 500/400 (Calcium 500 mg/400 IU Vitamin D3), chewable tablets, orally, twice, daily, on Days 15 through 28.	
Reporting group title	Test Group 2: Sequence CD
Reporting group description:	
Calcichew D3 500/800 (Calcium 500 mg/800 IU Vitamin D3) [C], chewable tablets, orally, once, daily, on Days 1 through 14, followed by Kalcipos-D (Calcium 500 mg/800 IU Vitamin D3) [D], chewable tablets, orally, once, daily, on Days 15 through 28.	
Reporting group title	Test Group 2: Sequence DC
Reporting group description:	
Kalcipos-D (Calcium 500 mg/800 IU Vitamin D3), chewable tablets, orally, once, daily, on Days 1 through 14, followed by, Calcichew D3 500/800 (Calcium 500 mg/800 IU Vitamin D3), chewable tablets, orally, once, daily, on Days 15 through 28.	
Subject analysis set title	United Kingdom: Calcichew D3 500/400
Subject analysis set type	Full analysis
Subject analysis set description:	
Calcichew D3 500/400 (Calcium 500 mg/400 IU Vitamin D3) [A], chewable tablets, orally, twice, daily, on Days 1 through 14 or Days 15 through 28.	
Subject analysis set title	United Kingdom: Adcal-D3
Subject analysis set type	Full analysis
Subject analysis set description:	
Adcal-D3 (Calcium 600 mg / 400 IU Vitamin D3), chewable tablets, orally, twice, daily, on Days 1 through 14 or Days 15 through 28.	
Subject analysis set title	Germany: Calcichew D3 500/800
Subject analysis set type	Full analysis

Subject analysis set description:

Calcichew D3 500/800 (Calcium 500 mg/800 IU Vitamin D3) [C], chewable tablets, orally, once, daily, on Days 1 through 14 or Days 15 through 28.

Subject analysis set title	Germany: Kalcipos-D
Subject analysis set type	Full analysis

Subject analysis set description:

Kalcipos-D (Calcium 500 mg/800 IU Vitamin D3), chewable tablets, orally, once, daily, on Days 1 through 14 or Days 15 through 28.

Subject analysis set title	United Kingdom: Calcichew D3 500/400
Subject analysis set type	Safety analysis

Subject analysis set description:

Calcichew D3 500/400 (Calcium 500 mg/400 IU Vitamin D3) [A], chewable tablets, orally, twice, daily, on Days 1 through 14 or Days 15 through 28.

Subject analysis set title	United Kingdom: Adcal-D3 Adcal-D3
Subject analysis set type	Safety analysis

Subject analysis set description:

Adcal-D3 (Calcium 600 mg / 400 IU Vitamin D3), chewable tablets, orally, twice, daily, on Days 1 through 14 or Days 15 through 28.

Subject analysis set title	Germany: Calcichew D3 500/800
Subject analysis set type	Safety analysis

Subject analysis set description:

Calcichew D3 500/800 (Calcium 500 mg/800 IU Vitamin D3) [C], chewable tablets, orally, once, daily, on Days 1 through 14 or Days 15 through 28.

Subject analysis set title	Germany: Kalcipos-D
Subject analysis set type	Safety analysis

Subject analysis set description:

Kalcipos-D (Calcium 500 mg/800 IU Vitamin D3), chewable tablets, orally, once, daily, on Days 1 through 14 or Days 15 through 28.

Subject analysis set title	Test Group 1: Total
Subject analysis set type	Full analysis

Subject analysis set description:

Calcichew D3 500/400 (Calcium 500 mg/400 IU Vitamin D3) [A], chewable tablets, orally, twice, daily, for 14 days in either Period 1 or 2 and Adcal-D3 (Calcium 600 mg / 400 IU Vitamin D3) [B], chewable tablets, orally, twice, daily, for 14 days in either Period 1 or 2.

Subject analysis set title	Test Group 2: Total
Subject analysis set type	Full analysis

Subject analysis set description:

Calcichew D3 500/800 (Calcium 500 mg/800 IU Vitamin D3) [C], chewable tablets, orally, once, daily, for 14 days in either Period 1 or 2 and Kalcipos-D (Calcium 500 mg/800 IU Vitamin D3) [D], chewable tablets, orally, for 14 days in either Period 1 or 2.

Primary: Percentage of Participants with a Preference for Each Treatment within Each Test Group

End point title	Percentage of Participants with a Preference for Each Treatment within Each Test Group[1]

End point description:

Preference was assessed by a 3 box questionnaire. Participants checked off one of the boxes: I prefer the first product that was tested, I prefer the second product that was tested or I have no preference. Test Group 1 (United Kingdom): Calcichew D3 is 500/400 and the comparator is Adcal-D3. Test Group 2 (Germany): Calcichew D3 is 500/800 and the comparator is Kalcipos-D.

Population Description: All randomized participants from the Full Analysis Set (FAS) who received at least 1 dose of study medication and responded to the preference questionnaire.

End point type	Primary

End point timeframe:

Day 28

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: Statistical Analysis not reported for this End Point.

End point values	Test Group 1: Sequence AB	Test Group 1: Sequence BA	Test Group 2: Sequence CD	Test Group 2: Sequence DC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	65	68	70
Units: percentage of participants				
number (not applicable)				
Preference for Calcichew D3	67.2	72.3	61.8	52.9
Preference for Comparator	28.1	12.3	29.4	37.1
No Preference	4.7	15.4	8.8	10

End point values	Test Group 1: Total	Test Group 2: Total		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	129	138		
Units: percentage of participants				
number (not applicable)				
Preference for Calcichew D3	69.8	57.2		
Preference for Comparator	20.2	33.3		
No Preference	10.1	9.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Product Acceptability after each 14 Day Dosing Period within Each Test Group

End point title	Product Acceptability after each 14 Day Dosing Period within Each Test Group

End point description:

Product acceptability was assessed by a 6 item questionnaire evaluating the characteristics of the product: gritty, chalky, sweet, ease of chew, ease of swallow and sticky. Using a 100 mm visual analog scale (VAS) the participant put a vertical line through each horizontal line that best describes their level of agreement with each item using a 0 to 100 scale where: 0=far left of the line (best) to 100= far right of the line (worst). Linear mixed model was used for analysis with treatment and period as fixed effects and participants as a random effect.

Population description: The FAS included all randomized participants who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Day 14 and Day 28

End point values	United Kingdom: Calcichew D3 500/400	United Kingdom: Adcal-D3	Germany: Calcichew D3 500/800	Germany: Kalcipos-D
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	138	138	138	138
Units: mm				
least squares mean (standard error)				
Gritty	19.2 (± 2.18)	24.6 (± 2.18)	28.4 (± 2.28)	27 (± 2.28)
Chalky	23.2 (± 2.49)	41.1 (± 2.49)	25.9 (± 2.43)	29.9 (± 2.43)
Sweet/Bitter	32.5 (± 1.74)	34.5 (± 1.74)	34.1 (± 1.67)	38 (± 1.67)
Chew	8.1 (± 1.62)	18.1 (± 1.62)	12.2 (± 1.77)	19 (± 1.78)
Swallow	10.8 (± 2.01)	20.5 (± 2)	11 (± 1.88)	19.5 (± 1.89)
Sticky	6.1 (± 1.22)	10.9 (± 1.22)	8.2 (± 1.16)	8.4 (± 1.16)

Statistical analyses

No statistical analyses for this end point

Secondary: Product Tolerability Expressed as the Percentage of Participants who Experience at Least One Treatment-Emergent Adverse Event within each Test Group

End point title	Product Tolerability Expressed as the Percentage of Participants who Experience at Least One Treatment-Emergent Adverse Event within each Test Group

End point description:

An Adverse Event (AE) is defined as any untoward medical occurrence in a clinical investigation participant administered a drug; it does not necessarily have to have a causal relationship with this treatment. A treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset that occurs after receiving study drug.

The Safety Analysis Set included all randomized participants who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Day 1 to Day 28

End point values	United Kingdom: Calcichew D3 500/400	United Kingdom: Adcal-D3 Adcal-D3	Germany: Calcichew D3 500/800	Germany: Kalcipos-D
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	135	136	138	138
Units: percentage of participants				
number (not applicable)	14.8	9.6	5.1	4.3

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of the study drug to the last dose of study drug (Up to 28 days)

Adverse event reporting additional description:

At each visit the investigator had to document any occurrence of adverse events and abnormal laboratory findings. Any event spontaneously reported by the participant or observed by the investigator was recorded, irrespective of the relation to study treatment.
Safety Set included all participants who received at least 1 dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	United Kingdom: Calcichew D3 500/400

Reporting group description:

Calcichew D3 500/400 (Calcium 500 mg/400 IU Vitamin D3) [A], chewable tablets, orally, twice, daily, on Days 1 through 14 or Days 15 through 28.

Reporting group title	United Kingdom: Adcal-D3

Reporting group description:

Adcal-D3 (Calcium 600 mg / 400 IU Vitamin D3), chewable tablets, orally, twice, daily, on Days 1 through 14 or Days 15 through 28.

Reporting group title	Germany: Calcichew D3 500/800

Reporting group description:

Calcichew D3 500/800 (Calcium 500 mg/800 IU Vitamin D3) [C], chewable tablets, orally, once, daily, on Days 1 through 14 or Days 15 through 28.

Reporting group title	Germany: Kalcipos-D

Reporting group description:

Kalcipos-D (Calcium 500 mg/800 IU Vitamin D3), chewable tablets, orally, once, daily, on Days 1 through 14 or Days 15 through 28.

Serious adverse events	United Kingdom: Calcichew D3 500/400	United Kingdom: Adcal-D3	Germany: Calcichew D3 500/800
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 135 (0.74%)	0 / 136 (0.00%)	0 / 138 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	1 / 135 (0.74%)	0 / 136 (0.00%)	0 / 138 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Germany: Kalcipos-		

	D		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 138 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	0 / 138 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	United Kingdom: Calcichew D3 500/400	United Kingdom: Adcal-D3	Germany: Calcichew D3 500/800
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 135 (0.74%)	5 / 136 (3.68%)	0 / 138 (0.00%)
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 135 (0.74%)	5 / 136 (3.68%)	0 / 138 (0.00%)
occurrences (all)	1	5	0

Non-serious adverse events	Germany: Kalcipos-D		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 138 (0.00%)		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 138 (0.00%)		
occurrences (all)	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