



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 | v2 (current) |
| This version publication date | 18 November 2016 |
| First version publication date | 18 June 2016 |
| Version creation reason | • Correction of full data set Update |

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 endpoint

| 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.

| | |
|----------------|-----------|
| 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 | 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