Clinical trial results:
Randomised, double-blind, double-dummy, multicentre trial to evaluate the efficacy and safety of three different weekly dosages of calcifediol versus placebo in subjects with either vitamin D deficiency or insufficiency.

Summary

EudraCT number	2020-001099-14
Trial protocol	FR SK CZ BG IT
Global end of trial date	25 April 2023

Results information

Result version number	v1 (current)
This version publication date	20 September 2024
First version publication date	20 September 2024

Trial information

Trial identification

Sponsor protocol code	HIDR-0320/DR

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	FAES FARMA, S.A.
Sponsor organisation address	Avenida Autonomía 10, Leioa (Bizkaia), Spain, 48940
Public contact	Clinical Research Derpartment, FAES FARMA, S.A., 0034 663626137, clinical_rd@faes.es
Scientific contact	Clinical Research Derpartment, FAES FARMA, S.A., 0034 663626137, clinical_rd@faes.es

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	11 July 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 July 2022
Global end of trial reached?	Yes
Global end of trial date	25 April 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The general objective of this clinical study was to determine the efficacy and safety of 3 new weekly doses (75 mcg, 100 mcg and 125 mcg) of calcifediol SGCs compared to placebo.

Protection of trial subjects:

The study is conducted in accordance with the Declaration of Helsinki (2013) as well as with the valid national laws of the participating countries, with the International Conference on Harmonisation (ICH) Harmonised Tripartite Guideline for Good Clinical Practice (GCP) (E6), and with the Commission Directives 2001/20/EC, 2005/28/EC and 2001/83/EC.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 December 2020
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	Bulgaria: 243
Country: Number of subjects enrolled	Czechia: 316
Country: Number of subjects enrolled	France: 31
Country: Number of subjects enrolled	Italy: 35
Country: Number of subjects enrolled	Serbia: 108
Country: Number of subjects enrolled	Slovakia: 320
Country: Number of subjects enrolled	Spain: 235
Worldwide total number of subjects	1288
EEA total number of subjects	1180

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)	926
From 65 to 84 years	347
85 years and over	15

Subject disposition

Recruitment

Recruitment details:

A total of 1288 subjects were enrolled at 55 study sites in 7 countries (Bulgaria, Czech Republic, Spain, France, Italy, Serbia, Slovakia). Of these, 614 subjects failed screening. In total 674 subjects of both cohorts (Cohort1: 398 subjects, Cohort2: 276 subjects) were randomised.

Pre-assignment

Screening details:

614 subjects failed screening. In total 674 subjects of both cohorts (Cohort1: 398 subjects, Cohort2: 276 subjects) were randomised by 31 MAR 2022.

Pre-assignment period milestones

Number of subjects started	1288
Number of subjects completed	674

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Consent withdrawn by subject: 10
Reason: Number of subjects	Protocol deviation: 1
Reason: Number of subjects	Ineligibility/developm. of an excl./withdr. crit.: 549
Reason: Number of subjects	Lost to follow-up: 1
Reason: Number of subjects	At the specific request of the sponsor: 1
Reason: Number of subjects	Other: 50
Reason: Number of subjects	Persisting 25-OH-D level ≤ 10 ng/mL: 2

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Overall - Placebo

Arm description:

Oral administration of 75/100/125 mcg Calcifediol SGC matching Placebo once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Placebo SGCs (75 mcg, 100 mcg, 125 mcg) oral administration once per week

Arm title	Overall - Calcifediol 75 mcg

Arm description:

Oral administration of 75 mcg Calcifediol SGC once per week on Sunday morning (at least 48 hours

before next blood sample extraction) during the treatment period

Arm type	Active comparator
Investigational medicinal product name	Calcifediol (25-OH-D)
Investigational medicinal product code	Calcifediol
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Oral administration of 75 mcg Calcifediol SGC once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period

Arm title	Overall - Calcifediol 100 mcg

Arm description:

Oral administration of 100 mcg Calcifediol SGC once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period

Arm type	Active comparator
Investigational medicinal product name	Calcifediol (25-OH-D)
Investigational medicinal product code	Calcifediol
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Oral administration of 100 mcg Calcifediol SGC once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period

Arm title	Overall - Calcifediol 125 mcg

Arm description:

Oral administration of 125 mcg Calcifediol SGC once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period

Arm type	Active comparator
Investigational medicinal product name	Calcifediol (25-OH-D)
Investigational medicinal product code	Calcifediol
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Oral administration of 125 mcg Calcifediol SGC once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period

Number of subjects in period 1[1]	Overall - Placebo	Overall - Calcifediol 75 mcg	Overall - Calcifediol 100 mcg
Started	130	159	271
Completed	130	159	271

Number of subjects in period 1[1]	Overall - Calcifediol 125 mcg
Started	114
Completed	114

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Number of subjects in the baseline period are defined as subjects who met all the inclusion criteria and none of the exclusion criteria. Of the 1288 subjects enrolled in the trial, 614 subjects failed screening. In total 674 subjects of both cohorts (Cohort1: 398 subjects, Cohort2: 276 subjects) were randomised.

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment - Placebo

Arm description:

Oral administration of 75/100/125 mcg Calcifediol SGC matching Placebo once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Placebo SGCs (75 mcg, 100 mcg, 125 mcg) oral administration once per week

Arm title	Treatment - Calcifediol 75 mcg

Arm description:

Oral administration of 75 mcg Calcifediol SGC once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period

Arm type	Active comparator
Investigational medicinal product name	Calcifediol (25-OH-D)
Investigational medicinal product code	Calcifediol
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Oral administration of 75 mcg Calcifediol SGC once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period

Arm title	Treatment - Calcifediol 100 mcg

Arm description:

Oral administration of 100 mcg Calcifediol SGC once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period

Arm type	Active comparator
Investigational medicinal product name	Calcifediol (25-OH-D)
Investigational medicinal product code	Calcifediol
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Oral administration of 100 mcg Calcifediol SGC once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period

Arm title	Treatment - Calcifediol 125 mcg

Arm description:

Oral administration of 125 mcg Calcifediol SGC once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period

Arm type	Active comparator
Investigational medicinal product name	Calcifediol (25-OH-D)
Investigational medicinal product code	Calcifediol
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Oral administration of 125 mcg Calcifediol SGC once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period

Number of subjects in period 2	Treatment - Placebo	Treatment - Calcifediol 75 mcg	Treatment - Calcifediol 100 mcg
Started	130	159	271
Completed	107	142	239
Not completed	23	17	32
Consent withdrawn by subject	8	6	15
Adverse event, non-fatal	1	4	2
Persisting 25-OH-D level ≤ 10 ng/mL	1	-	-
Other	1	-	-
Pregnancy	1	-	1
At the specific request of the sponsor	2	-	-
Ineligibility/developm. of an excl. /withdr. crit.	5	3	5
Use of prohibited concomitant medication	2	3	6
Lost to follow-up	2	1	2
Protocol deviation	-	-	1

Number of subjects in period 2	Treatment - Calcifediol 125 mcg
Started	114
Completed	94
Not completed	20
Consent withdrawn by subject	7
Adverse event, non-fatal	4
Persisting 25-OH-D level ≤ 10 ng/mL	-
Other	-
Pregnancy	-
At the specific request of the sponsor	-
Ineligibility/developm. of an excl. /withdr. crit.	9

Use of prohibited concomitant medication	-
Lost to follow-up	-
Protocol deviation	-

Period 3

Period 3 title	Safety Follow-Up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Safety Follow-Up - Placebo

Arm description:

Oral administration of 75/100/125 mcg Calcifediol SGC matching Placebo once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period.

Due to technical issues of EudrCT database only the 107 subjects of the Placebo treated arm could be stated, that completed treatment period and did Follow-Up Visit 8. In total 117 subjects of this arm had a Follow-Up Visit 8.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Placebo SGCs (75 mcg, 100 mcg, 125 mcg) oral administration once per week

Arm title	Safety Follow-Up - Calcifediol 75 mcg

Arm description:

Oral administration of 75 mcg Calcifediol SGC once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period.

Due to technical issues of EudrCT database only the 142 subjects treated with Calcifediol 75 mcg could be stated, that completed treatment period and did Follow-Up Visit 8. In total 150 subjects of this arm had a Follow-Up Visit 8.

Arm type	Active comparator
Investigational medicinal product name	Calcifediol (25-OH-D)
Investigational medicinal product code	Calcifediol
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Oral administration of 75 mcg Calcifediol SGC once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period

Arm title	Safety Follow-Up - Calcifediol 100 mcg

Arm description:

Oral administration of 100 mcg Calcifediol SGC once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period.

Due to technical issues of EudrCT database only the 239 subjects treated with Calcifediol 100 mcg could be stated, that completed treatment period and did Follow-Up Visit 8. In total 248 subjects of this arm had a Follow-Up Visit 8.

Arm type	Active comparator
Investigational medicinal product name	Calcifediol (25-OH-D)
Investigational medicinal product code	Calcifediol
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Oral administration of 100 mcg Calcifediol SGC once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period

Arm title	Safety Follow-Up - Calcifediol 125 mcg

Arm description:

Oral administration of 125 mcg Calcifediol SGC once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period.

Due to technical issues of EudrCT database only the 94 subjects treated with Calcifediol 125 mcg could be stated, that completed treatment period and did Follow-Up Visit 8. In total 102 subjects of this arm had a Follow-Up Visit 8.

Arm type	Active comparator
Investigational medicinal product name	Calcifediol (25-OH-D)
Investigational medicinal product code	Calcifediol
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Oral administration of 125 mcg Calcifediol SGC once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period

Number of subjects in period 3	Safety Follow-Up - Placebo	Safety Follow-Up - Calcifediol 75 mcg	Safety Follow-Up - Calcifediol 100 mcg
Started	107	142	239
Completed	107	142	239

Number of subjects in period 3	Safety Follow-Up - Calcifediol 125 mcg
Started	94
Completed	94

Baseline characteristics

Subject analysis sets	
Subject analysis set title	Overall - Placebo x Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects who took at least one dose of IP	
Subject analysis set title	Overall - Calcifediol 75 mcg x Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects who took at least one dose of IP	
Subject analysis set title	Overall - Calcifediol 100 mcg x Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects who took at least one dose of IP	
Subject analysis set title	Overall - Calcifediol 125 mcg x Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects who took at least one dose of IP	
Subject analysis set title	Overall - Placebo x Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects who took at least one dose of IP and who had at least one post baseline assessment of the primary efficacy measurement (25OH-D level).	
Subject analysis set title	Overall - Calcifediol 75 mcg x Full Analsysis Set
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects who took at least one dose of IP and who had at least one post baseline assessment of the primary efficacy measurement (25OH-D level).	
Subject analysis set title	Overall - Calcifediol 100 mcg x Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects who took at least one dose of IP and who had at least one post baseline assessment of the primary efficacy measurement (25OH-D level).	
Subject analysis set title	Overall - Calcifediol 125 mcg x Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects who took at least one dose of IP and who had at least one post baseline assessment of the primary efficacy measurement (25OH-D level).	
Subject analysis set title	Overall - Placebo x Safety Set (Cohort 1)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects of of Safety Set, having 25-OH-D baseline level > 10 to < 20 ng/mL	
Subject analysis set title	Overall - Calcifediol 75 mcg x Safety Set (Cohort 1)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects of of Safety Set, having 25-OH-D baseline level > 10 to < 20 ng/mL	
Subject analysis set title	Overall - Calcifediol 100 mcg x Safety Set (Cohort 1)
Subject analysis set type	Sub-group analysis

Subject analysis set description:	
Subjects of of Safety Set, having 25-OH-D baseline level > 10 to < 20 ng/mL	
Subject analysis set title	Overall - Placebo x Safety Set (Cohort 2)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects of Safety Set, having 25-OH-D baseline level ≤ 10 ng/mL	
Subject analysis set title	Overall - Calcifediol 100 mcg x Safety Set (Cohort 2)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects of Safety Set, having 25-OH-D baseline level ≤ 10 ng/mL	
Subject analysis set title	Overall - Calcifediol 125 mcg x Safety Set (Cohort 2)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects of Safety Set, having 25-OH-D baseline level ≤ 10 ng/mL	
Subject analysis set title	Overall - Placebo x Full Analysis Set (Cohort 1)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects of of Full Analysis Set, having 25-OH-D baseline level > 10 to < 20 ng/mL	
Subject analysis set title	Overall - Calcifediol 75 mcg x Full Analysis Set (Cohort 1)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects of of Full Analysis Set, having 25-OH-D baseline level > 10 to < 20 ng/mL	
Subject analysis set title	Overall - Calcifediol 100 mcg x Full Analysis Set (Cohort 1)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects of of Full Analysis Set, having 25-OH-D baseline level > 10 to < 20 ng/mL	
Subject analysis set title	Overall - Placebo x Full Analysis Set (Cohort 2)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects of Full Analysis Set, having 25-OH-D baseline level ≤ 10 ng/mL	
Subject analysis set title	Overall - Calcifediol 100 mcg x Full Analysis Set (Cohort 2)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects of Full Analysis Set, having 25-OH-D baseline level ≤ 10 ng/mL	
Subject analysis set title	Overall - Calcifediol 125 mcg x Full Analysis Set (Cohort 2)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects of Full Analysis Set, having 25-OH-D baseline level ≤ 10 ng/mL	

Reporting group values	Overall - Placebo x Safety Set	Overall - Calcifediol 75 mcg x Safety Set	Overall - Calcifediol 100 mcg x Safety Set
Number of subjects	128	158	266
Age Categorical			
Age Categorical Characteristic			
Units: Subjects			
In Utero Preterm newborn- gestational age < 37 wk Newborns (0-27days) Infants and toddlers (28days – 23months) Children (2-11 years)			

Adolescents (12-17 year) From 18 - 64 years From 65 – 84 years Over 85 years			
Age Continuous			
Age Continuous Characteristic			
Units: years arithmetic mean standard deviation	±	±	±
Gender Categorical			
Gender Categorical Characteristic			
Units: Subjects			
Female Male			

Reporting group values	Overall - Calcifediol 125 mcg x Safety Set	Overall - Placebo x Full Analysis Set	Overall - Calcifediol 75 mcg x Full Analsysis Set
Number of subjects	113	128	156
Age Categorical			
Age Categorical Characteristic			
Units: Subjects			
In Utero Preterm newborn- gestational age < 37 wk Newborns (0-27days) Infants and toddlers (28days – 23months) Children (2-11 years) Adolescents (12-17 year) From 18 - 64 years From 65 – 84 years Over 85 years			
Age Continuous			
Age Continuous Characteristic			
Units: years arithmetic mean standard deviation	±	±	±
Gender Categorical			
Gender Categorical Characteristic			
Units: Subjects			
Female Male			

Reporting group values	Overall - Calcifediol 100 mcg x Full Analysis Set	Overall - Calcifediol 125 mcg x Full Analysis Set	Overall - Placebo x Safety Set (Cohort 1)
Number of subjects	263	110	73
Age Categorical			
Age Categorical Characteristic			
Units: Subjects			
In Utero Preterm newborn- gestational age < 37 wk			0 0

Newborns (0-27days)			0
Infants and toddlers (28days – 23months)			0
Children (2-11 years)			0
Adolescents (12-17 year)			0
From 18 - 64 years			58
From 65 – 84 years			15
Over 85 years			0
Age Continuous			
Age Continuous Characteristic			
Units: years			
arithmetic mean			50.1
standard deviation	±	±	± 15.43
Gender Categorical			
Gender Categorical Characteristic			
Units: Subjects			
Female			51
Male			22

Reporting group values	Overall - Calcifediol 75 mcg x Safety Set (Cohort 1)	Overall - Calcifediol 100 mcg x Safety Set (Cohort 1)	Overall - Placebo x Safety Set (Cohort 2)
Number of subjects	158	162	55
Age Categorical			
Age Categorical Characteristic			
Units: Subjects			
In Utero	0	0	0
Preterm newborn- gestational age < 37 wk	0	0	0
Newborns (0-27days)	0	0	0
Infants and toddlers (28days – 23months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 year)	0	0	0
From 18 - 64 years	119	122	42
From 65 – 84 years	39	40	13
Over 85 years	0	0	0
Age Continuous			
Age Continuous Characteristic			
Units: years			
arithmetic mean	52.7	51.3	53.8
standard deviation	± 15.81	± 16.43	± 12.9
Gender Categorical			
Gender Categorical Characteristic			
Units: Subjects			
Female	124	116	43
Male	34	46	12

Reporting group values	Overall - Calcifediol 100 mcg x Safety Set (Cohort 2)	Overall - Calcifediol 125 mcg x Safety Set (Cohort 2)	Overall - Placebo x Full Analysis Set (Cohort 1)
Number of subjects	104	113	73

Age Categorical			
Age Categorical Characteristic			
Units: Subjects			
In Utero	0	0	
Preterm newborn- gestational age < 37 wk	0	0	
Newborns (0-27days)	0	0	
Infants and toddlers (28days – 23months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 year)	0	0	
From 18 - 64 years	71	75	
From 65 – 84 years	33	35	
Over 85 years	0	3	
Age Continuous			
Age Continuous Characteristic			
Units: years			
arithmetic mean	55.4	56.3	
standard deviation	± 15.97	± 16.41	±
Gender Categorical			
Gender Categorical Characteristic			
Units: Subjects			
Female	79	79	
Male	25	34	

Reporting group values	Overall - Calcifediol 75 mcg x Full Analysis Set (Cohort 1)	Overall - Calcifediol 100 mcg x Full Analysis Set (Cohort 1)	Overall - Placebo x Full Analysis Set (Cohort 2)
Number of subjects	156	159	55
Age Categorical			
Age Categorical Characteristic			
Units: Subjects			
In Utero			
Preterm newborn- gestational age < 37 wk			
Newborns (0-27days)			
Infants and toddlers (28days – 23months)			
Children (2-11 years)			
Adolescents (12-17 year)			
From 18 - 64 years			
From 65 – 84 years			
Over 85 years			
Age Continuous			
Age Continuous Characteristic			
Units: years			
arithmetic mean			
standard deviation	±	±	±
Gender Categorical			
Gender Categorical Characteristic			
Units: Subjects			
Female			
Male			

Reporting group values	Overall - Calcifediol 100 mcg x Full Analysis Set (Cohort 2)	Overall - Calcifediol 125 mcg x Full Analysis Set (Cohort 2)	
Number of subjects	104	110	
Age Categorical			
Age Categorical Characteristic			
Units: Subjects			
In Utero Preterm newborn- gestational age < 37 wk Newborns (0-27days) Infants and toddlers (28days – 23months) Children (2-11 years) Adolescents (12-17 year) From 18 - 64 years From 65 – 84 years Over 85 years			
Age Continuous			
Age Continuous Characteristic			
Units: years arithmetic mean standard deviation	±	±	
Gender Categorical			
Gender Categorical Characteristic			
Units: Subjects			
Female Male			

End points

End points reporting groups

Reporting group title	Overall - Placebo
Reporting group description:	
Oral administration of 75/100/125 mcg Calcifediol SGC matching Placebo once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period	
Reporting group title	Overall - Calcifediol 75 mcg
Reporting group description:	
Oral administration of 75 mcg Calcifediol SGC once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period	
Reporting group title	Overall - Calcifediol 100 mcg
Reporting group description:	
Oral administration of 100 mcg Calcifediol SGC once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period	
Reporting group title	Overall - Calcifediol 125 mcg
Reporting group description:	
Oral administration of 125 mcg Calcifediol SGC once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period	
Reporting group title	Treatment - Placebo
Reporting group description:	
Oral administration of 75/100/125 mcg Calcifediol SGC matching Placebo once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period	
Reporting group title	Treatment - Calcifediol 75 mcg
Reporting group description:	
Oral administration of 75 mcg Calcifediol SGC once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period	
Reporting group title	Treatment - Calcifediol 100 mcg
Reporting group description:	
Oral administration of 100 mcg Calcifediol SGC once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period	
Reporting group title	Treatment - Calcifediol 125 mcg
Reporting group description:	
Oral administration of 125 mcg Calcifediol SGC once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period	
Reporting group title	Safety Follow-Up - Placebo
Reporting group description:	
Oral administration of 75/100/125 mcg Calcifediol SGC matching Placebo once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period. Due to technical issues of EudrCT database only the 107 subjects of the Placebo treated arm could be stated, that completed treatment period and did Follow-Up Visit 8. In total 117 subjects of this arm had a Follow-Up Visit 8.	
Reporting group title	Safety Follow-Up - Calcifediol 75 mcg
Reporting group description:	
Oral administration of 75 mcg Calcifediol SGC once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period. Due to technical issues of EudrCT database only the 142 subjects treated with Calcifediol 75 mcg could be stated, that completed treatment period and did Follow-Up Visit 8. In total 150 subjects of this arm had a Follow-Up Visit 8.	
Reporting group title	Safety Follow-Up - Calcifediol 100 mcg
Reporting group description:	
Oral administration of 100 mcg Calcifediol SGC once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period. Due to technical issues of EudrCT database only the 239 subjects treated with Calcifediol 100 mcg could	

be stated, that completed treatment period and did Follow-Up Visit 8. In total 248 subjects of this arm had a Follow-Up Visit 8.

Reporting group title	Safety Follow-Up - Calcifediol 125 mcg

Reporting group description:

Oral administration of 125 mcg Calcifediol SGC once per week on Sunday morning (at least 48 hours before next blood sample extraction) during the treatment period.

Due to technical issues of EudrCT database only the 94 subjects treated with Calcifediol 125 mcg could be stated, that completed treatment period and did Follow-Up Visit 8. In total 102 subjects of this arm had a Follow-Up Visit 8.

Subject analysis set title	Overall - Placebo x Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects who took at least one dose of IP

Subject analysis set title	Overall - Calcifediol 75 mcg x Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects who took at least one dose of IP

Subject analysis set title	Overall - Calcifediol 100 mcg x Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects who took at least one dose of IP

Subject analysis set title	Overall - Calcifediol 125 mcg x Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects who took at least one dose of IP

Subject analysis set title	Overall - Placebo x Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects who took at least one dose of IP and who had at least one post baseline assessment of the primary efficacy measurement (25OH-D level).

Subject analysis set title	Overall - Calcifediol 75 mcg x Full Analsysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects who took at least one dose of IP and who had at least one post baseline assessment of the primary efficacy measurement (25OH-D level).

Subject analysis set title	Overall - Calcifediol 100 mcg x Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects who took at least one dose of IP and who had at least one post baseline assessment of the primary efficacy measurement (25OH-D level).

Subject analysis set title	Overall - Calcifediol 125 mcg x Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects who took at least one dose of IP and who had at least one post baseline assessment of the primary efficacy measurement (25OH-D level).

Subject analysis set title	Overall - Placebo x Safety Set (Cohort 1)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects of of Safety Set, having 25-OH-D baseline level > 10 to < 20 ng/mL

Subject analysis set title	Overall - Calcifediol 75 mcg x Safety Set (Cohort 1)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects of of Safety Set, having 25-OH-D baseline level > 10 to < 20 ng/mL

Subject analysis set title	Overall - Calcifediol 100 mcg x Safety Set (Cohort 1)

Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects of of Safety Set, having 25-OH-D baseline level > 10 to < 20 ng/mL	
Subject analysis set title	Overall - Placebo x Safety Set (Cohort 2)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects of Safety Set, having 25-OH-D baseline level ≤ 10 ng/mL	
Subject analysis set title	Overall - Calcifediol 100 mcg x Safety Set (Cohort 2)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects of Safety Set, having 25-OH-D baseline level ≤ 10 ng/mL	
Subject analysis set title	Overall - Calcifediol 125 mcg x Safety Set (Cohort 2)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects of Safety Set, having 25-OH-D baseline level ≤ 10 ng/mL	
Subject analysis set title	Overall - Placebo x Full Analysis Set (Cohort 1)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects of of Full Analysis Set, having 25-OH-D baseline level > 10 to < 20 ng/mL	
Subject analysis set title	Overall - Calcifediol 75 mcg x Full Analysis Set (Cohort 1)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects of of Full Analysis Set, having 25-OH-D baseline level > 10 to < 20 ng/mL	
Subject analysis set title	Overall - Calcifediol 100 mcg x Full Analysis Set (Cohort 1)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects of of Full Analysis Set, having 25-OH-D baseline level > 10 to < 20 ng/mL	
Subject analysis set title	Overall - Placebo x Full Analysis Set (Cohort 2)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects of Full Analysis Set, having 25-OH-D baseline level ≤ 10 ng/mL	
Subject analysis set title	Overall - Calcifediol 100 mcg x Full Analysis Set (Cohort 2)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects of Full Analysis Set, having 25-OH-D baseline level ≤ 10 ng/mL	
Subject analysis set title	Overall - Calcifediol 125 mcg x Full Analysis Set (Cohort 2)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects of Full Analysis Set, having 25-OH-D baseline level ≤ 10 ng/mL	

Primary: 25-OH-D response level of ≥ 30 ng/mL at endpoint (Visit 4 [Week 16])

End point title	25-OH-D response level of ≥ 30 ng/mL at endpoint (Visit 4 [Week 16])
End point description: The primary endpoint of this trial was 25-OH-D response level of ≥ 30 ng/mL at endpoint (Visit 4 [Week 16]). Subjects were allocated to two cohorts based on their 25-OH-D baseline level at Visit 1	
End point type	Primary
End point timeframe: 16 weeks	

End point values	Overall - Placebo x Full Analysis Set (Cohort 1)	Overall - Calcifediol 75 mcg x Full Analysis Set (Cohort 1)	Overall - Calcifediol 100 mcg x Full Analysis Set (Cohort 1)	Overall - Placebo x Full Analysis Set (Cohort 2)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	73	156	159	55
Units: [%]				
number (not applicable)				
Response Rate	11	74.4000000000	89.9	0

End point values	Overall - Calcifediol 100 mcg x Full Analysis Set (Cohort 2)	Overall - Calcifediol 125 mcg x Full Analysis Set (Cohort 2)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	104	110		
Units: [%]				
number (not applicable)				
Response Rate	49	76.4000000000		

Statistical analyses

Statistical analysis title	z-test

Statistical analysis description:

The percentage of 25-OH-D responders was analysed using a large-sample normal approximation test of proportions, also known as a z-test. For the primary efficacy analysis, responders were those subjects who achieved 25 OH D levels of ≥ 30 ng/mL at Visit 4/16 weeks of treatment. For confirmatory testing of 25-OH-D response rate, as a primary approach, subjects with missing 25-OH-D level at 16 weeks for any reason, including discontinuation prior to Visit 4, were regarded as non-responders.

Comparison groups	Overall - Calcifediol 100 mcg x Full Analysis Set (Cohort 1) v Overall - Placebo x Full Analysis Set (Cohort 1)
Number of subjects included in analysis	232
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	z-test

Statistical analysis title	z-test

Statistical analysis description:

The percentage of 25-OH-D responders was analysed using a large-sample normal approximation test of proportions, also known as a z-test. For the primary efficacy analysis, responders were those subjects

who achieved 25 OH D levels of ≥ 30 ng/mL at Visit 4/16 weeks of treatment. For confirmatory testing of 25-OH-D response rate, as a primary approach, subjects with missing 25-OH-D level at 16 weeks for any reason, including discontinuation prior to Visit 4, were regarded as non-responders.

Comparison groups	Overall - Calcifediol 75 mcg x Full Analysis Set (Cohort 1) v Overall - Placebo x Full Analysis Set (Cohort 1)
Number of subjects included in analysis	229
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	z-test

Statistical analysis title	z-test

Statistical analysis description:

The percentage of 25-OH-D responders was analysed using a large-sample normal approximation test of proportions, also known as a z-test. For the primary efficacy analysis, responders were those subjects who achieved 25 OH D levels of ≥ 30 ng/mL at Visit 4/16 weeks of treatment. For confirmatory testing of 25-OH-D response rate, as a primary approach, subjects with missing 25-OH-D level at 16 weeks for any reason, including discontinuation prior to Visit 4, were regarded as non-responders.

Comparison groups	Overall - Calcifediol 100 mcg x Full Analysis Set (Cohort 2) v Overall - Placebo x Full Analysis Set (Cohort 2)
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	z-test

Statistical analysis title	z-test

Statistical analysis description:

The percentage of 25-OH-D responders was analysed using a large-sample normal approximation test of proportions, also known as a z-test. For the primary efficacy analysis, responders were those subjects who achieved 25 OH D levels of ≥ 30 ng/mL at Visit 4/16 weeks of treatment. For confirmatory testing of 25-OH-D response rate, as a primary approach, subjects with missing 25-OH-D level at 16 weeks for any reason, including discontinuation prior to Visit 4, were regarded as non-responders.

Comparison groups	Overall - Calcifediol 125 mcg x Full Analysis Set (Cohort 2) v Overall - Placebo x Full Analysis Set (Cohort 2)
Number of subjects included in analysis	165
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	z-test

Statistical analysis title	z-test

Statistical analysis description:

The percentage of 25-OH-D responders was analysed using a large-sample normal approximation test of proportions, also known as a z-test. For the primary efficacy analysis, responders were those subjects who achieved 25 OH D levels of ≥ 30 ng/mL at Visit 4/16 weeks of treatment. For confirmatory testing of 25-OH-D response rate, as a primary approach, subjects with missing 25-OH-D level at 16 weeks for any reason, including discontinuation prior to Visit 4, were regarded as non-responders.

Comparison groups	Overall - Calcifediol 125 mcg x Full Analysis Set (Cohort 2) v

	Overall - Calcifediol 100 mcg x Full Analysis Set (Cohort 2)
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	z-test

Statistical analysis title	z-test

Statistical analysis description:

The percentage of 25-OH-D responders was analysed using a large-sample normal approximation test of proportions, also known as a z-test. For the primary efficacy analysis, responders were those subjects who achieved 25 OH D levels of ≥ 30 ng/mL at Visit 4/16 weeks of treatment. For confirmatory testing of 25-OH-D response rate, as a primary approach, subjects with missing 25-OH-D level at 16 weeks for any reason, including discontinuation prior to Visit 4, were regarded as non-responders.

Comparison groups	Overall - Calcifediol 100 mcg x Full Analysis Set (Cohort 1) v Overall - Calcifediol 75 mcg x Full Analysis Set (Cohort 1)
Number of subjects included in analysis	315
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002
Method	z-test

Primary: 25-OH-D response level of ≥ 20 ng/mL at endpoint (Visit 4 [Week 16])

End point title	25-OH-D response level of ≥ 20 ng/mL at endpoint (Visit 4 [Week 16])

End point description:

The primary endpoint of this trial was 25-OH-D response level of ≥ 20 ng/mL at endpoint (Visit 4 [Week 16]). Subjects were allocated to two cohorts based on their 25-OH-D baseline level at Visit 1

End point type	Primary

End point timeframe:

16 weeks

End point values	Overall - Placebo x Full Analysis Set (Cohort 1)	Overall - Calcifediol 75 mcg x Full Analysis Set (Cohort 1)	Overall - Calcifediol 100 mcg x Full Analysis Set (Cohort 1)	Overall - Placebo x Full Analysis Set (Cohort 2)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	73	156	159	55
Units: [%]				
number (not applicable)				
Response Rate	50.7	93.6	98.7	7.3

End point values	Overall - Calcifediol 100 mcg x Full Analysis Set (Cohort 2)	Overall - Calcifediol 125 mcg x Full Analysis Set (Cohort 2)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	104	110		
Units: [%]				
number (not applicable)				
Response Rate	92.3	91.8		

Statistical analyses

Statistical analysis title	z-test

Statistical analysis description:

The percentage of 25-OH-D responders was analysed using a large-sample normal approximation test of proportions, also known as a z-test. For the primary efficacy analysis, responders were those subjects who achieved 25 OH D levels of ≥ 20 ng/mL at Visit 4/16 weeks of treatment. For confirmatory testing of 25-OH-D response rate, as a primary approach, subjects with missing 25-OH-D level at 16 weeks for any reason, including discontinuation prior to Visit 4, were regarded as non-responders.

Comparison groups	Overall - Calcifediol 100 mcg x Full Analysis Set (Cohort 1) v Overall - Placebo x Full Analysis Set (Cohort 1)
Number of subjects included in analysis	232
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	z-test

Statistical analysis title	z-test

Statistical analysis description:

The percentage of 25-OH-D responders was analysed using a large-sample normal approximation test of proportions, also known as a z-test. For the primary efficacy analysis, responders were those subjects who achieved 25 OH D levels of ≥ 20 ng/mL at Visit 4/16 weeks of treatment. For confirmatory testing of 25-OH-D response rate, as a primary approach, subjects with missing 25-OH-D level at 16 weeks for any reason, including discontinuation prior to Visit 4, were regarded as non-responders.

Comparison groups	Overall - Calcifediol 100 mcg x Full Analysis Set (Cohort 1) v Overall - Calcifediol 75 mcg x Full Analysis Set (Cohort 1)
Number of subjects included in analysis	315
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.0002
Method	z-test

Statistical analysis title	z-test

Statistical analysis description:

The percentage of 25-OH-D responders was analysed using a large-sample normal approximation test of proportions, also known as a z-test. For the primary efficacy analysis, responders were those subjects who achieved 25 OH D levels of ≥ 20 ng/mL at Visit 4/16 weeks of treatment. For confirmatory testing of 25-OH-D response rate, as a primary approach, subjects with missing 25-OH-D level at 16 weeks for

any reason, including discontinuation prior to Visit 4, were regarded as non-responders.

Comparison groups	Overall - Calcifediol 125 mcg x Full Analysis Set (Cohort 2) v Overall - Calcifediol 100 mcg x Full Analysis Set (Cohort 2)
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.0464
Method	z-test

Statistical analysis title	z-test

Statistical analysis description:

The percentage of 25-OH-D responders was analysed using a large-sample normal approximation test of proportions, also known as a z-test. For the primary efficacy analysis, responders were those subjects who achieved 25 OH D levels of ≥ 20 ng/mL at Visit 4/16 weeks of treatment. For confirmatory testing of 25-OH-D response rate, as a primary approach, subjects with missing 25-OH-D level at 16 weeks for any reason, including discontinuation prior to Visit 4, were regarded as non-responders.

Comparison groups	Overall - Calcifediol 100 mcg x Full Analysis Set (Cohort 2) v Overall - Placebo x Full Analysis Set (Cohort 2)
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	z-test

Statistical analysis title	z-test

Statistical analysis description:

The percentage of 25-OH-D responders was analysed using a large-sample normal approximation test of proportions, also known as a z-test. For the primary efficacy analysis, responders were those subjects who achieved 25 OH D levels of ≥ 20 ng/mL at Visit 4/16 weeks of treatment. For confirmatory testing of 25-OH-D response rate, as a primary approach, subjects with missing 25-OH-D level at 16 weeks for any reason, including discontinuation prior to Visit 4, were regarded as non-responders.

Comparison groups	Overall - Calcifediol 125 mcg x Full Analysis Set (Cohort 2) v Overall - Calcifediol 100 mcg x Full Analysis Set (Cohort 2)
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8946
Method	z-test

Statistical analysis title	z-test

Statistical analysis description:

The percentage of 25-OH-D responders was analysed using a large-sample normal approximation test of proportions, also known as a z-test. For the primary efficacy analysis, responders were those subjects who achieved 25 OH D levels of ≥ 20 ng/mL at Visit 4/16 weeks of treatment. For confirmatory testing of 25-OH-D response rate, as a primary approach, subjects with missing 25-OH-D level at 16 weeks for any reason, including discontinuation prior to Visit 4, were regarded as non-responders.

Comparison groups	Overall - Calcifediol 75 mcg x Full Analysis Set (Cohort 1) v Overall - Placebo x Full Analysis Set (Cohort 1)

Number of subjects included in analysis	229
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	z-test

Statistical analysis title	z-test

Statistical analysis description:

The percentage of 25-OH-D responders was analysed using a large-sample normal approximation test of proportions, also known as a z-test. For the primary efficacy analysis, responders were those subjects who achieved 25 OH D levels of ≥ 20 ng/mL at Visit 4/16 weeks of treatment. For confirmatory testing of 25-OH-D response rate, as a primary approach, subjects with missing 25-OH-D level at 16 weeks for any reason, including discontinuation prior to Visit 4, were regarded as non-responders.

Comparison groups	Overall - Calcifediol 125 mcg x Full Analysis Set (Cohort 2) v Overall - Placebo x Full Analysis Set (Cohort 2)
Number of subjects included in analysis	165
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	z-test

Adverse events

Adverse events information

Timeframe for reporting adverse events:

In this clinical trial TEAEs were defined as all untoward events with onset or worsening after the first intake of the IP until 30 days after the last IP intake.

Adverse event reporting additional description:

In this clinical trial TEAEs were defined as all untoward events with onset or worsening after the first intake of the IP until 30 days after the last IP intake.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Overall - Placebo x Safety Set (Cohort 1)

Reporting group description:

Subjects of of Safety Set, having 25-OH-D baseline level > 10 to < 20 ng/mL

Reporting group title	Overall - Calcifediol 75 mcg/week x Safety Set (Cohort 1)

Reporting group description:

Subjects of of Safety Set, having 25-OH-D baseline level > 10 to < 20 ng/mL

Reporting group title	Overall - Calcifediol 125 mcg/week x Safety Set (Cohort 2)

Reporting group description:

Subjects of Safety Set, having 25-OH-D baseline level ≤ 10 ng/mL

Reporting group title	Overall - Placebo x Safety Set (Cohort 2)

Reporting group description:

Subjects of Safety Set, having 25-OH-D baseline level ≤ 10 ng/mL

Reporting group title	Overall - Calcifediol 100 mcg/week x Safety Set (Cohort 2)

Reporting group description:

Subjects of Safety Set, having 25-OH-D baseline level ≤ 10 ng/mL

Reporting group title	Overall - Calcifediol 100 mcg/week x Safety Set (Cohort 1)

Reporting group description:

Subjects of of Safety Set, having 25-OH-D baseline level > 10 to < 20 ng/mL

Serious adverse events	Overall - Placebo x Safety Set (Cohort 1)	Overall - Calcifediol 75 mcg/week x Safety Set (Cohort 1)	Overall - Calcifediol 125 mcg/week x Safety Set (Cohort 2)
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 73 (8.22%)	7 / 158 (4.43%)	4 / 113 (3.54%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive ductal breast carcinoma			

subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Meniscus injury			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Craniocerebral injury			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	1 / 73 (1.37%)	0 / 158 (0.00%)	0 / 113 (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
Deep vein thrombosis			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dementia			

subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Optic neuritis			
subjects affected / exposed	1 / 73 (1.37%)	0 / 158 (0.00%)	0 / 113 (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
General disorders and administration site conditions			
Sudden death			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peptic ulcer haemorrhage			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incarcerated umbilical hernia			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 73 (1.37%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 73 (1.37%)	0 / 158 (0.00%)	0 / 113 (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
Renal and urinary disorders			
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 73 (2.74%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	1 / 73 (1.37%)	0 / 158 (0.00%)	0 / 113 (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
Erysipelas			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			

subjects affected / exposed	1 / 73 (1.37%)	0 / 158 (0.00%)	0 / 113 (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
Pneumonia			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Overall - Placebo x Safety Set (Cohort 2)	Overall - Calcifediol 100 mcg/week x Safety Set (Cohort 2)	Overall - Calcifediol 100 mcg/week x Safety Set (Cohort 1)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 55 (5.45%)	3 / 104 (2.88%)	3 / 162 (1.85%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Meniscus injury			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Craniocerebral injury			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic aneurysm			

subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dementia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Optic neuritis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Sudden death			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peptic ulcer haemorrhage			

subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incarcerated umbilical hernia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	1 / 55 (1.82%)	0 / 104 (0.00%)	0 / 162 (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
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			

subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	1 / 55 (1.82%)	0 / 104 (0.00%)	0 / 162 (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
COVID-19 pneumonia			
subjects affected / exposed	1 / 55 (1.82%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Overall - Placebo x Safety Set (Cohort 1)	Overall - Calcifediol 75 mcg/week x Safety Set (Cohort 1)	Overall - Calcifediol 125 mcg/week x Safety Set (Cohort 2)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 73 (36.99%)	52 / 158 (32.91%)	40 / 113 (35.40%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Skin papilloma			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Aortic arteriosclerosis			
subjects affected / exposed	1 / 73 (1.37%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Hot flush			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	0 / 73 (0.00%)	5 / 158 (3.16%)	2 / 113 (1.77%)
occurrences (all)	0	6	2
Hypotension			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	1 / 113 (0.88%)
occurrences (all)	0	1	1
Thrombosis			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	3	0
Post thrombotic syndrome			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Thrombophlebitis			
subjects affected / exposed	1 / 73 (1.37%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Peripheral venous disease			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	0 / 73 (0.00%)	2 / 158 (1.27%)	1 / 113 (0.88%)
occurrences (all)	0	2	1
Vaccination site pruritus			

subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 73 (0.00%)	2 / 158 (1.27%)	0 / 113 (0.00%)
occurrences (all)	0	2	0
Hyperpyrexia			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	0	2
Fatigue			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Cyst			
subjects affected / exposed	1 / 73 (1.37%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Chest pain			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 73 (0.00%)	2 / 158 (1.27%)	1 / 113 (0.88%)
occurrences (all)	0	2	1
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Allergy to animal			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Cervical dysplasia			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Gynaecomastia			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	0	1
Sexual dysfunction			

subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Prostatism			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	0	1
Vulvovaginal discomfort			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Vulvovaginal inflammation			
subjects affected / exposed	1 / 73 (1.37%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	0 / 73 (0.00%)	2 / 158 (1.27%)	0 / 113 (0.00%)
occurrences (all)	0	2	0
Cough			
subjects affected / exposed	0 / 73 (0.00%)	2 / 158 (1.27%)	0 / 113 (0.00%)
occurrences (all)	0	2	0
Bronchitis chronic			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Asthmatic crisis			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Asthma			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Pharyngeal disorder			

subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	0	1
Confusional state			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	0	1
Mixed anxiety and depressive disorder			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	2 / 73 (2.74%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	2	0	1
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	0	1
Blood 25-hydroxycholecalciferol decreased			
subjects affected / exposed	7 / 73 (9.59%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	8	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 73 (1.37%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Blood parathyroid hormone increased			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0

Occult blood			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Heart rate irregular			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	1 / 113 (0.88%)
occurrences (all)	0	1	1
Coronavirus test positive			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Blood pressure diastolic increased			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Blood potassium increased			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Transaminases increased			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	0	1
Weight increased			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Fibula fracture			
subjects affected / exposed	1 / 73 (1.37%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Contusion			

subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Ankle fracture			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Head injury			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	0	1
Post vaccination syndrome			
subjects affected / exposed	1 / 73 (1.37%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Limb fracture			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Extrasystoles			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Cardiac failure			
subjects affected / exposed	1 / 73 (1.37%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Palpitations			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Carotid artery stenosis			
subjects affected / exposed	1 / 73 (1.37%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Carotid arteriosclerosis			

subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Sciatica			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	1 / 113 (0.88%)
occurrences (all)	0	1	1
Piriformis syndrome			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Migraine			
subjects affected / exposed	1 / 73 (1.37%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Hypersomnia			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	1 / 113 (0.88%)
occurrences (all)	0	1	1
Essential tremor			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Epilepsy			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	0	1
Carpal tunnel syndrome			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	0	1

Secondary thrombocytosis			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	0	1
Iron deficiency anaemia			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Tinnitus			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Ear pain			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Cerumen impaction			
subjects affected / exposed	1 / 73 (1.37%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	1	1	0
Eye disorders			
Vitreous floaters			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Conjunctival haemorrhage			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Blepharitis			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			

Constipation			
subjects affected / exposed	2 / 73 (2.74%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	2	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	1 / 113 (0.88%)
occurrences (all)	0	1	1
Abdominal pain lower			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	0 / 73 (0.00%)	2 / 158 (1.27%)	0 / 113 (0.00%)
occurrences (all)	0	2	0
Abdominal distension			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Dry mouth			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Pancreatic steatosis			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	0	1
Odynophagia			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	1 / 73 (1.37%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	1	0	1

Hyperchlorhydria			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Hiatus hernia			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Gingival bleeding			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Gastric ulcer			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Dyspepsia			
subjects affected / exposed	0 / 73 (0.00%)	2 / 158 (1.27%)	0 / 113 (0.00%)
occurrences (all)	0	2	0
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	1 / 73 (1.37%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	1	0	1
Cholelithiasis			
subjects affected / exposed	1 / 73 (1.37%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	2	0
Perioral dermatitis			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			

subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Ecchymosis			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Angioedema			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Acne			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	0	1
Skin lesion			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Urinary tract discomfort			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	0	1
Renal cyst			
subjects affected / exposed	1 / 73 (1.37%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Renal colic			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Microalbuminuria			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0

Dysuria			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Chronic kidney disease			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	0	1
Nephropathy			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	0	1
Endocrine disorders			
Autoimmune thyroiditis			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Thyroid mass			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Hypothyroidism			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Hyperparathyroidism secondary			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Fibromyalgia			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Limb discomfort			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Lumbar spinal stenosis			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Muscle contracture			

subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	1 / 113 (0.88%)
occurrences (all)	0	1	1
Connective tissue disorder			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Chondropathy			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 73 (0.00%)	4 / 158 (2.53%)	1 / 113 (0.88%)
occurrences (all)	0	5	1
Arthritis			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	0 / 73 (0.00%)	3 / 158 (1.90%)	4 / 113 (3.54%)
occurrences (all)	0	4	5
Muscular weakness			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 73 (0.00%)	2 / 158 (1.27%)	0 / 113 (0.00%)
occurrences (all)	0	2	0
Osteitis			
subjects affected / exposed	1 / 73 (1.37%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Osteopenia			
subjects affected / exposed	1 / 73 (1.37%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	1 / 73 (1.37%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	1	1	0
Pain in jaw			

subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	0	1
Patellofemoral pain syndrome			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Plantar fasciitis			
subjects affected / exposed	0 / 73 (0.00%)	2 / 158 (1.27%)	0 / 113 (0.00%)
occurrences (all)	0	2	0
Rheumatoid arthritis			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Spinal pain			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Synovial cyst			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Tendonitis			
subjects affected / exposed	0 / 73 (0.00%)	2 / 158 (1.27%)	0 / 113 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Abscess limb			
subjects affected / exposed	1 / 73 (1.37%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Abscess			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	3 / 113 (2.65%)
occurrences (all)	0	1	3
Acute sinusitis			
subjects affected / exposed	1 / 73 (1.37%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Balanitis candida			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0

Bronchitis			
subjects affected / exposed	2 / 73 (2.74%)	2 / 158 (1.27%)	0 / 113 (0.00%)
occurrences (all)	2	3	0
COVID-19			
subjects affected / exposed	6 / 73 (8.22%)	13 / 158 (8.23%)	18 / 113 (15.93%)
occurrences (all)	6	15	18
Clostridium difficile colitis			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 73 (0.00%)	3 / 158 (1.90%)	0 / 113 (0.00%)
occurrences (all)	0	3	0
Dermatophytosis of nail			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Erysipelas			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Escherichia urinary tract infection			
subjects affected / exposed	1 / 73 (1.37%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Fungal infection			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Furuncle			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis viral			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Genital herpes			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	0	1

Helicobacter infection			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Herpes simplex			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Herpes zoster			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 73 (0.00%)	2 / 158 (1.27%)	0 / 113 (0.00%)
occurrences (all)	0	2	0
Laryngitis			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Lyme disease			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Onychomycosis			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection			
subjects affected / exposed	1 / 73 (1.37%)	2 / 158 (1.27%)	1 / 113 (0.88%)
occurrences (all)	1	2	1
Post viral fatigue syndrome			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	2 / 73 (2.74%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	4	1	0

Sinusitis			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	0	1
Schistosomiasis			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection viral			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Oral infection			
subjects affected / exposed	1 / 73 (1.37%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Otitis externa			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Periodontitis			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	1 / 73 (1.37%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Tonsillitis streptococcal			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	1 / 73 (1.37%)	3 / 158 (1.90%)	2 / 113 (1.77%)
occurrences (all)	1	3	2

Upper respiratory tract infection			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Tracheobronchitis			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Tooth abscess			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Obesity			
subjects affected / exposed	0 / 73 (0.00%)	2 / 158 (1.27%)	0 / 113 (0.00%)
occurrences (all)	0	2	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Hypernatraemia			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	0	1
Hypercholesterolaemia			
subjects affected / exposed	0 / 73 (0.00%)	2 / 158 (1.27%)	0 / 113 (0.00%)
occurrences (all)	0	2	0
Hypercalcaemia			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	2 / 113 (1.77%)
occurrences (all)	0	1	2
Folate deficiency			
subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Fluid retention			

subjects affected / exposed	0 / 73 (0.00%)	1 / 158 (0.63%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Dyslipidaemia			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Diabetes mellitus			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	4 / 113 (3.54%)
occurrences (all)	0	0	4
Overweight			
subjects affected / exposed	0 / 73 (0.00%)	0 / 158 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Overall - Placebo x Safety Set (Cohort 2)	Overall - Calcifediol 100 mcg/week x Safety Set (Cohort 2)	Overall - Calcifediol 100 mcg/week x Safety Set (Cohort 1)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 55 (38.18%)	32 / 104 (30.77%)	66 / 162 (40.74%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Vascular disorders			
Aortic arteriosclerosis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	2 / 55 (3.64%)	1 / 104 (0.96%)	2 / 162 (1.23%)
occurrences (all)	2	1	2
Hypotension			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Thrombosis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0

Post thrombotic syndrome			
subjects affected / exposed	1 / 55 (1.82%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	1	0	0
Thrombophlebitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Peripheral venous disease			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	2
Asthenia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	0 / 162 (0.00%)
occurrences (all)	0	1	0
Vaccination site pruritus			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	2 / 162 (1.23%)
occurrences (all)	0	0	2
Hyperpyrexia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Cyst			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	1 / 55 (1.82%)	1 / 104 (0.96%)	1 / 162 (0.62%)
occurrences (all)	1	1	1
Oedema peripheral			

subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	0 / 162 (0.00%)
occurrences (all)	0	1	0
Allergy to animal			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Cervical dysplasia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Gynaecomastia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Sexual dysfunction			
subjects affected / exposed	1 / 55 (1.82%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	1	0	0
Prostatism			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal discomfort			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal inflammation			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	0 / 162 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	1 / 55 (1.82%)	1 / 104 (0.96%)	0 / 162 (0.00%)
occurrences (all)	1	1	0
Dysphonia			

subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	1 / 55 (1.82%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	1	0	1
Bronchitis chronic			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Asthmatic crisis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	0 / 162 (0.00%)
occurrences (all)	0	2	0
Asthma			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Pharyngeal disorder			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Rhinitis allergic			
subjects affected / exposed	0 / 55 (0.00%)	2 / 104 (1.92%)	1 / 162 (0.62%)
occurrences (all)	0	2	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 55 (1.82%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	1	0	0
Confusional state			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Mixed anxiety and depressive disorder			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	1 / 162 (0.62%)
occurrences (all)	0	1	1
Depression			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	1 / 162 (0.62%)
occurrences (all)	0	1	1
Investigations			

Blood creatinine increased			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Blood 25-hydroxycholecalciferol decreased			
subjects affected / exposed	5 / 55 (9.09%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	5	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	2 / 162 (1.23%)
occurrences (all)	0	0	2
Alanine aminotransferase increased			
subjects affected / exposed	1 / 55 (1.82%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	1	0	1
Blood parathyroid hormone increased			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Occult blood			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Heart rate irregular			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	0 / 162 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	2 / 162 (1.23%)
occurrences (all)	0	0	2
Coronavirus test positive			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Blood pressure diastolic increased			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	1 / 162 (0.62%)
occurrences (all)	0	1	1
Blood potassium increased			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			

subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	2 / 162 (1.23%)
occurrences (all)	0	0	2
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	1 / 55 (1.82%)	0 / 104 (0.00%)	2 / 162 (1.23%)
occurrences (all)	1	0	2
Fibula fracture			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Ankle fracture			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Head injury			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Post vaccination syndrome			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Limb fracture			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Ligament sprain			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	0 / 162 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			

Extrasystoles			
subjects affected / exposed	1 / 55 (1.82%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	1	0	0
Cardiac failure			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Carotid artery stenosis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	1	0	0
Carotid arteriosclerosis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Piriformis syndrome			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	0 / 162 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Hypersomnia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Headache			

subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	1 / 162 (0.62%)
occurrences (all)	0	1	1
Essential tremor			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Epilepsy			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	0 / 162 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Carpal tunnel syndrome			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	2
Secondary thrombocytosis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Leukopenia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 55 (1.82%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	1	0	0
Tinnitus			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Ear pain			

subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	0 / 162 (0.00%)
occurrences (all)	0	1	0
Cerumen impaction			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Vitreous floaters			
subjects affected / exposed	1 / 55 (1.82%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	1	0	0
Vision blurred			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Conjunctival haemorrhage			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Blepharitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Abdominal pain lower			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	1 / 162 (0.62%)
occurrences (all)	0	1	1
Abdominal distension			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Diarrhoea			

subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	2 / 162 (1.23%)
occurrences (all)	0	0	2
Dry mouth			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	1 / 55 (1.82%)	1 / 104 (0.96%)	0 / 162 (0.00%)
occurrences (all)	1	1	0
Pancreatic steatosis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Odynophagia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 55 (1.82%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	1	0	0
Hyperchlorhydria			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Hiatus hernia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Haemorrhoids			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	1 / 55 (1.82%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	1	0	0
Gastric ulcer			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			

subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	1	0	0
Cholelithiasis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	0 / 162 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	2 / 162 (1.23%)
occurrences (all)	0	0	2
Rash			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Perioral dermatitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Hyperhidrosis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	1 / 162 (0.62%)
occurrences (all)	0	1	1
Erythema			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	1	0	0
Dermatitis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	1	0	1
Angioedema			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Acne			

subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Urinary tract discomfort			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Renal cyst			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Renal colic			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Pollakiuria			
subjects affected / exposed	1 / 55 (1.82%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	1	0	0
Microalbuminuria			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	0 / 162 (0.00%)
occurrences (all)	0	1	0
Chronic kidney disease			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Nephropathy			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Autoimmune thyroiditis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Thyroid mass			

subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	0 / 162 (0.00%)
occurrences (all)	0	1	0
Hypothyroidism			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	0 / 162 (0.00%)
occurrences (all)	0	1	0
Hyperparathyroidism secondary			
subjects affected / exposed	1 / 55 (1.82%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Fibromyalgia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Intervertebral disc protrusion			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Limb discomfort			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Lumbar spinal stenosis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Muscle contracture			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Connective tissue disorder			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Chondropathy			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	0 / 162 (0.00%)
occurrences (all)	0	1	0
Back pain			

subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	2 / 162 (1.23%)
occurrences (all)	0	1	2
Arthritis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	2 / 162 (1.23%)
occurrences (all)	0	0	2
Arthralgia			
subjects affected / exposed	2 / 55 (3.64%)	0 / 104 (0.00%)	3 / 162 (1.85%)
occurrences (all)	2	0	3
Muscular weakness			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Osteitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Osteopenia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	1 / 162 (0.62%)
occurrences (all)	0	1	1
Pain in jaw			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Patellofemoral pain syndrome			
subjects affected / exposed	1 / 55 (1.82%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	1	0	0
Plantar fasciitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Rheumatoid arthritis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	1	0	0
Spinal pain			

subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Synovial cyst			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Tendonitis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Abscess			
subjects affected / exposed	1 / 55 (1.82%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	1 / 162 (0.62%)
occurrences (all)	0	1	1
Acute sinusitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Balanitis candida			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	0 / 162 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	2 / 162 (1.23%)
occurrences (all)	0	1	3
COVID-19			
subjects affected / exposed	4 / 55 (7.27%)	9 / 104 (8.65%)	18 / 162 (11.11%)
occurrences (all)	4	9	18
Clostridium difficile colitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	0 / 162 (0.00%)
occurrences (all)	0	1	0

Cystitis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	1 / 162 (0.62%)
occurrences (all)	0	1	1
Dermatophytosis of nail			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	0 / 162 (0.00%)
occurrences (all)	0	1	0
Erysipelas			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Escherichia urinary tract infection			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Fungal infection			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	2 / 162 (1.23%)
occurrences (all)	0	0	2
Furuncle			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Genital herpes			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Helicobacter infection			
subjects affected / exposed	1 / 55 (1.82%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	1	0	0
Herpes simplex			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	1 / 162 (0.62%)
occurrences (all)	0	1	1
Oral herpes			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	2 / 162 (1.23%)
occurrences (all)	0	0	3

Laryngitis			
subjects affected / exposed	1 / 55 (1.82%)	1 / 104 (0.96%)	0 / 162 (0.00%)
occurrences (all)	1	1	0
Lyme disease			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 55 (0.00%)	2 / 104 (1.92%)	1 / 162 (0.62%)
occurrences (all)	0	2	1
Onychomycosis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	1 / 55 (1.82%)	2 / 104 (1.92%)	3 / 162 (1.85%)
occurrences (all)	1	2	3
Respiratory tract infection			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	2 / 162 (1.23%)
occurrences (all)	0	0	2
Post viral fatigue syndrome			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Tonsillitis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	1 / 162 (0.62%)
occurrences (all)	0	1	1
Sinusitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Schistosomiasis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Respiratory tract infection viral			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	0 / 162 (0.00%)
occurrences (all)	0	1	0

Oral infection			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	0 / 162 (0.00%)
occurrences (all)	0	1	0
Otitis externa			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Periodontitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Tonsillitis streptococcal			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Viral infection			
subjects affected / exposed	1 / 55 (1.82%)	1 / 104 (0.96%)	2 / 162 (1.23%)
occurrences (all)	1	1	2
Urinary tract infection			
subjects affected / exposed	1 / 55 (1.82%)	0 / 104 (0.00%)	2 / 162 (1.23%)
occurrences (all)	1	0	2
Upper respiratory tract infection			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Tracheobronchitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	1 / 162 (0.62%)
occurrences (all)	0	1	1

Metabolism and nutrition disorders			
Obesity			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Hypertriglyceridaemia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Hypernatraemia			
subjects affected / exposed	1 / 55 (1.82%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	1	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	0 / 162 (0.00%)
occurrences (all)	0	1	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Folate deficiency			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Fluid retention			
subjects affected / exposed	0 / 55 (0.00%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	0	0	0
Dyslipidaemia			
subjects affected / exposed	1 / 55 (1.82%)	0 / 104 (0.00%)	0 / 162 (0.00%)
occurrences (all)	1	0	0
Diabetes mellitus			
subjects affected / exposed	0 / 55 (0.00%)	2 / 104 (1.92%)	5 / 162 (3.09%)
occurrences (all)	0	2	5
Overweight			
subjects affected / exposed	0 / 55 (0.00%)	1 / 104 (0.96%)	0 / 162 (0.00%)
occurrences (all)	0	1	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