Clinical trial results:
A Randomized, Double-blind, Multicenter, Parallel-arm Phase 3 Study to Compare the Efficacy, Pharmacodynamics, Safety, and Immunogenicity Between Bmab 1000 and Prolia in Postmenopausal Women with Osteoporosis

Summary

EudraCT number	2021-006545-36
Trial protocol	LV EE PL
Global end of trial date	12 June 2024

Results information

Result version number	v1 (current)
This version publication date	30 January 2026
First version publication date	30 January 2026

Trial information

Trial identification

Sponsor protocol code	B1000-PMO-03-G-02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05345691
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Biocon Biologics UK Limited
Sponsor organisation address	16, Great Queen Street, Covent Garden, London, United Kingdom, WC2B 5AH
Public contact	Rajesh CN, Senior Director, Therapeutic Area Head, Biocon Biologics Limited, 080 28082808, rajesh.cn@biocon.com
Scientific contact	Sarika Deodhar, Senior Director, Medical Lead, Biocon Biologics Limited, 080 28085302, Sarika.deodhar@biocon.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 July 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 December 2023
Global end of trial reached?	Yes
Global end of trial date	12 June 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To demonstrate equivalent efficacy between Bmab 1000 and Prolia based on percentage change from baseline (%CfB) at Week 52 in lumbar spine Bone mineral density (BMD) (Co-primary for EMA and Primary for US FDA)
- To demonstrate pharmacodynamic equivalence between Bmab 1000 and Prolia based on Area under the effect curve (AUEC) of the bone resorption marker Serum C-terminal telopeptide of Type 1 collagen (sCTX) from baseline to week 26 (Co-primary for EMA and secondary US FDA)

Protection of trial subjects:

This study was conducted in accordance with the protocol and consensus ethical principles derived from international guidelines, including those that have their origin in the Declaration of Helsinki, ICH E6(R2), EMA, FDA Code of Federal Regulations Title 21, applicable ICH GCP Guidelines, and other local applicable laws and regulations.

Background therapy:

Concomitant medications by ATC level and preferred name in Part 1 (SAF) and Part 2 (SAF-TP) were vitamin D NOS and calcium supplements: cholecalciferol, calcium carbonate, calcium, cholecalciferol, calcium carbonate. Other concomitant medications at the ATC level 4 were HMG-CoA reductase inhibitors; thyroid hormones; selective beta blocking agents; plain ACE inhibitors; anilides; propionic acid derivatives; and plain angiotensin II receptor blockers. Other concomitant medications by preferred name were levothyroxine sodium; rosuvastatin calcium; paracetamol; and bisoprolol fumarate.

Evidence for comparator:

Denosumab is marketed in the US and Europe by Amgen under the brand name Prolia as a single-use PFS containing 60 mg of denosumab in 1 mL of solution (60 mg/mL) and is being used as a reference treatment in this study.

Actual start date of recruitment	24 May 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 6
Country: Number of subjects enrolled	Poland: 438
Country: Number of subjects enrolled	Estonia: 22
Country: Number of subjects enrolled	Latvia: 13
Worldwide total number of subjects	479
EEA total number of subjects	473

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)	172
From 65 to 84 years	307
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 479 patients were randomized (238 and 241 patients in Bmab 1000 and Prolia treatment groups). A total of 478 and 435 patients received the first and second dose on Day 1 and at Week 26. 426 patients (218 and 208 patients in Bmab 1000 and Prolia treatment groups) completed Part 1 of the study and received the third dose at Week 52.

Pre-assignment

Screening details:

A total of 1219 patients were screened; of these, 740 patients were screened failure, and 479 patients were randomized in Part 1.
Screening Period was from Day -28 to Day -1.

Period 1

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

Blinding implementation details:

Part 1 - Double-Blind Active-Controlled Period from Week 0 [Day 1] to Week 52 Predose, including two doses of the study drug on Day 1 and at Week 26.
In Part 1, eligible patients were randomly assigned (1:1) to receive either Bmab 1000 (60 mg) or Prolia (60 mg) via SC injection on Day 1 (Week 0, the same date as randomization) and at Week 26. Patients were followed-up for 26 weeks after the second dose.

Arms

Are arms mutually exclusive?	Yes
Arm title	Bmab 1000

Arm description:

Part 1 - Bmab 1000

Arm type	Experimental
Investigational medicinal product name	Denosumab
Investigational medicinal product code	Bmab 1000
Other name	Denosumab
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Bmab 1000 (60 mg) was administered SC, preferably in the abdomen using a prefilled syringe of 60 mg/mL solution for injection on Day 1 and at Week 26.

Arm title	Prolia

Arm description:

Part 1 - Prolia

Arm type	Active comparator
Investigational medicinal product name	Prolia
Investigational medicinal product code	
Other name	Denosumab
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Prolia (60 mg) was administered SC, preferably in the abdomen using a prefilled syringe of 60 mg/mL solution for injection on Day 1 and at Week 26.

Number of subjects in period 1	Bmab 1000	Prolia
Started	238	241
Completed	218	208
Not completed	20	33
Adverse Event	4	3
Signifiant protocol violation (non-compliance)	1	3
Other	1	4
Investigator decision	-	2
Withdrawal of consent	13	19
Lost to follow-up	1	1
Not treated	-	1

Period 2	
Period 2 title	Part 2 - Transition Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Part 2 - Transition Period from Week 52 to Week 78 [end-of-study {EoS} Visit].

Arms	
Are arms mutually exclusive?	Yes
Arm title	Bmab 1000-Bmab 1000

Arm description:

Part 2 - Bmab 1000-Bmab 1000

Arm type	Experimental
Investigational medicinal product name	Denosumab
Investigational medicinal product code	Bmab 1000
Other name	Denosumab
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Bmab 1000 (60 mg) was administered SC, preferably in the abdomen using a prefilled syringe of 60 mg/mL solution for injection at Week 52.

Arm title	Prolia-Bmab 1000

Arm description:

Part 2 - Prolia-Bmab 1000

Arm type	Experimental

Investigational medicinal product name	Prolia-Bmab 1000
Investigational medicinal product code	
Other name	Denosumab
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Bmab 1000 (60 mg) was administered SC, preferably in the abdomen using a prefilled syringe of 60 mg/mL solution for injection at Week 52.

Arm title	Prolia-Prolia

Arm description:

Part 2 - Prolia-Prolia

Arm type	Active comparator
Investigational medicinal product name	Prolia
Investigational medicinal product code	
Other name	Denosumab
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Prolia (60 mg) was administered SC, preferably in the abdomen using a PFS of 60 mg/mL solution for injection at Week 52.

Number of subjects in period 2	Bmab 1000-Bmab 1000	Prolia-Bmab 1000	Prolia-Prolia
Started	218	104	104
Completed	216	103	103
Not completed	2	1	1
Withdrawal of consent	2	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Bmab 1000
Reporting group description: Part 1 - Bmab 1000	
Reporting group title	Prolia
Reporting group description: Part 1 - Prolia	

Reporting group values	Bmab 1000	Prolia	Total
Number of subjects	238	241	479
Age categorical Units: Subjects			
Adults (18-64 years)	84	88	172
From 65-84 years	154	153	307
Age continuous Units: years			
median	67.0	67.0	
full range (min-max)	55 to 78	55 to 79	-
Gender categorical Units: Subjects			
Female	238	241	479
Male	0	0	0

End points

End points reporting groups	
Reporting group title	Bmab 1000
Reporting group description: Part 1 - Bmab 1000	
Reporting group title	Prolia
Reporting group description: Part 1 - Prolia	
Reporting group title	Bmab 1000-Bmab 1000
Reporting group description: Part 2 - Bmab 1000-Bmab 1000	
Reporting group title	Prolia-Bmab 1000
Reporting group description: Part 2 - Prolia-Bmab 1000	
Reporting group title	Prolia-Prolia
Reporting group description: Part 2 - Prolia-Prolia	

Primary: %CfB at Week 52 in the lumbar spine BMD by DXA	
End point title	%CfB at Week 52 in the lumbar spine BMD by DXA
End point description: - Estimand 1a-EMA (Co-primary Efficacy): Difference in means (Bmab 1000 – Prolia) in % change from baseline in the lumbar spine BMD by DXA after 52 weeks in postmenopausal women with osteoporosis treated with SC injections every 6 months assuming that all women received 2 doses without any errors or deviations in dosing and without receipt of any other medications affecting bones except for vitamin D and calcium supplements. - Estimand 1a-US FDA (Efficacy): Difference in means (Bmab 1000 – Prolia) in composite endpoint of % CfB in the lumbar spine BMD by DXA after 52 weeks (for patients who died, the %CfB was taken as 0) in postmenopausal women with osteoporosis treated with SC injections every 6 months irrespective of discontinuation of the treatment for any reason, errors or deviations in dosing and whether any other osteoporosis medications were taken.	
End point type	Primary
End point timeframe: Baseline and Week 52	

End point values	Bmab 1000	Prolia		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	237	235		
Units: % change from baseline				
number (not applicable)	5.562	4.951		

Statistical analyses

Statistical analysis title	Statistical analysis
Comparison groups	Bmab 1000 v Prolia
Number of subjects included in analysis	472
Analysis specification	Pre-specified
Analysis type	equivalence
Method	Mixed models analysis
Parameter estimate	LS Mean Difference in %CfB Estimate
Point estimate	0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.095
upper limit	1.316

Primary: AUEC of sCTX from baseline to 26 weeks	
End point title	AUEC of sCTX from baseline to 26 weeks
End point description:	
Estimand 1b-EMA (Co-primary PD): Ratio of geometric means (Bmab 1000/Prolia) in AUEC in (fasted) sCTX up to 26 weeks in postmenopausal women with osteoporosis treated with a SC injection without any dosing error and no receipt of any other medications affecting bones except for vitamin D and calcium supplements.	
End point type	Primary
End point timeframe:	
Baseline to Week 26	

End point values	Bmab 1000	Prolia		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	237	235		
Units: day*pg/mL				
number (not applicable)				
Geometric LS Mean	11966.48	11490.23		

Statistical analyses

Statistical analysis title	Statistical analysis
Comparison groups	Bmab 1000 v Prolia
Number of subjects included in analysis	472
Analysis specification	Pre-specified
Analysis type	equivalence
Method	ANCOVA
Parameter estimate	Ratio of Geometric LS Means (%)
Point estimate	104.14

Confidence interval	
level	95 %
sides	2-sided
lower limit	97.76
upper limit	110.95

Adverse events

Adverse events information

Timeframe for reporting adverse events:

GoutAEs have been reported from the start of the Double-Blind Active-Controlled Period (Part 1, from Week 0 [Day 1] to Week 52 Predose) until the end of the Transition Period (Part 2, from Week 52 to Week 78 [end-of-study {EoS} Visit] - 18 months.

Adverse event reporting additional description:

A subject is counted once if the subject reported one or more events in summarization of total subjects with non-serious AEs, and summarization of SOCs and PTs.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Part 1 - Bmab 1000
Reporting group description: -	
Reporting group title	Part 1 - Prolia
Reporting group description: -	
Reporting group title	Part 2 - Bmab 1000-Bmab 1000
Reporting group description: -	
Reporting group title	Part 2 - Prolia-Bmab 1000
Reporting group description: -	
Reporting group title	Part 2 - Prolia-Prolia

Reporting group description: -

Serious adverse events	Part 1 - Bmab 1000	Part 1 - Prolia	Part 2 - Bmab 1000-Bmab 1000
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 238 (5.88%)	7 / 240 (2.92%)	5 / 218 (2.29%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (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
Clear cell renal cell carcinoma			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (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

Colon cancer			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (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
Pancreatic carcinoma			
subjects affected / exposed	2 / 238 (0.84%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	0 / 218 (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			
Non-cardiac chest pain			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Endometrial hyperplasia			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (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
Ovarian cyst			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (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
Uterine prolapse			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (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
Respiratory, thoracic and mediastinal disorders			
Allergic sinusitis			

subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (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
Psychiatric disorders			
Schizophrenia			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (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			
Arterial injury			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
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 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (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
Myocardial infarction			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (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
Atrial fibrillation			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	0 / 218 (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			
Cerebrovascular accident			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Dizziness			

subjects affected / exposed	2 / 238 (0.84%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Ear inflammation			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (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
Noninfective mastoiditis			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (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
Eye disorders			
Cataract			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (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
Barrett's oesophagus			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (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
Diverticulum intestinal			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (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
Inflammatory bowel disease			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (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

Gastric ulcer			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (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
Ureterolithiasis			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (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
Musculoskeletal and connective tissue disorders			
Musculoskeletal disorder			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (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
Osteoarthritis			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
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			
Staphylococcal sepsis			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (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
Urosepsis			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (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
Vestibular neuronitis			

subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (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
Diverticulitis			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	0 / 218 (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

Serious adverse events	Part 2 - Prolia-Bmab 1000	Part 2 - Prolia-Prolia	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 104 (1.92%)	2 / 104 (1.92%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clear cell renal cell carcinoma			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 104 (0.00%)	1 / 104 (0.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Endometrial hyperplasia			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine prolapse			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Allergic sinusitis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Schizophrenia			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Arterial injury			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			

Acute myocardial infarction			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 104 (0.00%)	1 / 104 (0.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Ear inflammation			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Noninfective mastoiditis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			

subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 104 (0.96%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Barrett's oesophagus			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inflammatory bowel disease			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue			

disorders			
Musculoskeletal disorder			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Staphylococcal sepsis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular neuronitis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	1 / 104 (0.96%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Part 1 - Bmab 1000	Part 1 - Prolia	Part 2 - Bmab 1000-Bmab 1000
Total subjects affected by non-serious adverse events			
subjects affected / exposed	141 / 238 (59.24%)	153 / 240 (63.75%)	50 / 218 (22.94%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Benign breast neoplasm			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Benign neoplasm of thyroid gland			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Breast cancer			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Clear cell renal cell carcinoma			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Colon cancer			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Haemangioma of liver			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Pancreatic carcinoma			
subjects affected / exposed	2 / 238 (0.84%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	2	0	0
Papillary cystadenoma lymphomatosum			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Uterine leiomyoma			
subjects affected / exposed	1 / 238 (0.42%)	2 / 240 (0.83%)	0 / 218 (0.00%)
occurrences (all)	1	2	0
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Aortic arteriosclerosis			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Essential hypertension			

subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	6 / 238 (2.52%)	6 / 240 (2.50%)	2 / 218 (0.92%)
occurrences (all)	6	6	2
Peripheral venous disease			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Phlebitis superficial			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Thrombosis			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Chest pain			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Exercise tolerance decreased			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	1 / 238 (0.42%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	1	1	0
Injection site erythema			
subjects affected / exposed	3 / 238 (1.26%)	4 / 240 (1.67%)	1 / 218 (0.46%)
occurrences (all)	3	4	1
Injection site pain			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Injection site swelling			

subjects affected / exposed	0 / 238 (0.00%)	2 / 240 (0.83%)	0 / 218 (0.00%)
occurrences (all)	0	2	0
Peripheral swelling			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences (all)	0	0	1
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 238 (0.00%)	2 / 240 (0.83%)	0 / 218 (0.00%)
occurrences (all)	0	2	0
Reproductive system and breast disorders			
Endometrial hyperplasia			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Genital haemorrhage			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Ovarian cyst			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	2	0	0
Uterine polyp			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Uterine prolapse			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Vulvovaginal pain			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			

Allergic sinusitis			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 238 (0.42%)	2 / 240 (0.83%)	0 / 218 (0.00%)
occurrences (all)	1	2	0
Cough			
subjects affected / exposed	2 / 238 (0.84%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	2	1	0
Epistaxis			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	2 / 238 (0.84%)	2 / 240 (0.83%)	0 / 218 (0.00%)
occurrences (all)	2	2	0
Paranasal sinus inflammation			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	1 / 218 (0.46%)
occurrences (all)	0	1	1
Pulmonary fibrosis			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Pulmonary mass			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Reflux laryngitis			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Rhinitis allergic			
subjects affected / exposed	2 / 238 (0.84%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	2	0	0
Upper respiratory tract inflammation			
subjects affected / exposed	1 / 238 (0.42%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	1	1	0
Sinus disorder			

subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences (all)	0	0	1
Psychiatric disorders			
Anxiety disorder			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Depression			
subjects affected / exposed	2 / 238 (0.84%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	2	1	0
Insomnia			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Schizophrenia			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	2	0
Sleep disorder			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Investigations			
Adjusted calcium decreased			
subjects affected / exposed	1 / 238 (0.42%)	3 / 240 (1.25%)	0 / 218 (0.00%)
occurrences (all)	1	3	0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 238 (0.42%)	1 / 240 (0.42%)	1 / 218 (0.46%)
occurrences (all)	1	1	1
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 238 (0.42%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	1	1	0
Blood calcium decreased			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	1 / 218 (0.46%)
occurrences (all)	0	1	1
Blood calcium increased			

subjects affected / exposed	2 / 238 (0.84%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	2	0	0
Blood cholesterol increased			
subjects affected / exposed	1 / 238 (0.42%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	1	1	0
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 238 (1.26%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences (all)	3	0	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Blood parathyroid hormone increased			
subjects affected / exposed	2 / 238 (0.84%)	6 / 240 (2.50%)	1 / 218 (0.46%)
occurrences (all)	2	6	1
Blood pressure increased			
subjects affected / exposed	0 / 238 (0.00%)	2 / 240 (0.83%)	0 / 218 (0.00%)
occurrences (all)	0	2	0
Blood urine present			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	1 / 218 (0.46%)
occurrences (all)	0	1	1
Hepatic enzyme increased			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	1 / 218 (0.46%)
occurrences (all)	0	1	1
Low density lipoprotein increased			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Weight increased			

subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Amylase increased			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences (all)	0	0	1
Blood glucose abnormal			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	0	0	0
Blood parathyroid hormone decreased			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	2 / 218 (0.92%)
occurrences (all)	0	0	2
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	2 / 238 (0.84%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	2	0	0
Fascial rupture			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Foot fracture			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Hand fracture			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Head injury			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Immunisation reaction			

subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Incision site pain			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Ligament sprain			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Limb injury			
subjects affected / exposed	1 / 238 (0.42%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	1	1	0
Lumbar vertebral fracture			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Meniscus injury			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Patella fracture			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Procedural pain			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Thoracic vertebral fracture			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Tooth fracture			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	1 / 218 (0.46%)
occurrences (all)	0	1	1
Arterial injury			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences (all)	0	0	1
Epicondylitis			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	0	0	0
Joint injury			

subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences (all)	0	0	2
Radius fracture			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences (all)	0	0	1
Spinal compression fracture			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences (all)	0	0	1
Tendon rupture			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences (all)	0	0	1
Forearm fracture			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Coronary artery disease			
subjects affected / exposed	1 / 238 (0.42%)	2 / 240 (0.83%)	0 / 218 (0.00%)
occurrences (all)	1	2	0
Mitral valve incompetence			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Myocardial infarction			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Pulmonary valve incompetence			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0

Tricuspid valve incompetence			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Atrial fibrillation			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Carpal tunnel syndrome			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Cerebrovascular accident			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Dementia Alzheimer's type			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	7 / 238 (2.94%)	10 / 240 (4.17%)	0 / 218 (0.00%)
occurrences (all)	7	11	0
Headache			
subjects affected / exposed	9 / 238 (3.78%)	8 / 240 (3.33%)	4 / 218 (1.83%)
occurrences (all)	10	9	4
Hypoaesthesia			
subjects affected / exposed	1 / 238 (0.42%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	1	1	0
Memory impairment			
subjects affected / exposed	0 / 238 (0.00%)	2 / 240 (0.83%)	0 / 218 (0.00%)
occurrences (all)	0	2	0
Migraine			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Muscle contractions involuntary			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Neuralgia			

subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Neuropathy peripheral			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Sciatica			
subjects affected / exposed	3 / 238 (1.26%)	3 / 240 (1.25%)	0 / 218 (0.00%)
occurrences (all)	4	3	0
Syncope			
subjects affected / exposed	0 / 238 (0.00%)	2 / 240 (0.83%)	0 / 218 (0.00%)
occurrences (all)	0	2	0
Sinus headache			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Leukopenia			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Lymphadenitis			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Macrocytosis			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Neutropenia			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Thrombocytopenia			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Anaemia			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0

Ear and labyrinth disorders			
Deafness unilateral			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Ear inflammation			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Noninfective mastoiditis			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Tinnitus			
subjects affected / exposed	0 / 238 (0.00%)	2 / 240 (0.83%)	0 / 218 (0.00%)
occurrences (all)	0	2	0
Ear pruritus			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences (all)	0	0	1
Ear pain			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences (all)	0	0	1
Eye disorders			
Cataract			
subjects affected / exposed	2 / 238 (0.84%)	2 / 240 (0.83%)	1 / 218 (0.46%)
occurrences (all)	2	2	1
Eye pain			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Retinal tear			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Retinoschisis			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences (all)	0	0	1
Eye haemorrhage			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis allergic			

subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 238 (0.42%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	1	1	0
Abdominal pain upper			
subjects affected / exposed	2 / 238 (0.84%)	3 / 240 (1.25%)	0 / 218 (0.00%)
occurrences (all)	2	4	0
Angular cheilitis			
subjects affected / exposed	0 / 238 (0.00%)	2 / 240 (0.83%)	0 / 218 (0.00%)
occurrences (all)	0	2	0
Barrett's oesophagus			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	2	0	0
Chronic gastritis			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	4 / 238 (1.68%)	2 / 240 (0.83%)	0 / 218 (0.00%)
occurrences (all)	4	2	0
Dental caries			
subjects affected / exposed	0 / 238 (0.00%)	2 / 240 (0.83%)	0 / 218 (0.00%)
occurrences (all)	0	2	0
Diarrhoea			
subjects affected / exposed	1 / 238 (0.42%)	3 / 240 (1.25%)	1 / 218 (0.46%)
occurrences (all)	1	3	1
Diverticulum intestinal			
subjects affected / exposed	0 / 238 (0.00%)	2 / 240 (0.83%)	0 / 218 (0.00%)
occurrences (all)	0	2	0
Dyspepsia			
subjects affected / exposed	1 / 238 (0.42%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	1	1	0
Food poisoning			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0

Gastric polyps			
subjects affected / exposed	0 / 238 (0.00%)	2 / 240 (0.83%)	0 / 218 (0.00%)
occurrences (all)	0	2	0
Gastritis			
subjects affected / exposed	1 / 238 (0.42%)	1 / 240 (0.42%)	1 / 218 (0.46%)
occurrences (all)	1	1	1
Gastrointestinal disorder			
subjects affected / exposed	1 / 238 (0.42%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	1	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences (all)	1	0	1
Gingival pain			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Haemorrhoids			
subjects affected / exposed	1 / 238 (0.42%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	1	1	0
Inflammatory bowel disease			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Oesophageal perforation			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Gastric ulcer			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences (all)	0	0	1
Hyperaesthesia teeth			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences (all)	0	0	1
Large intestine polyp			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	0	0	0

Mesenteric cyst			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences (all)	0	0	1
Oesophageal ulcer			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences (all)	0	0	1
Reflux gastritis			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Hepatic cyst			
subjects affected / exposed	0 / 238 (0.00%)	2 / 240 (0.83%)	0 / 218 (0.00%)
occurrences (all)	0	2	0
Hepatic steatosis			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Cholecystitis			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Actinic keratosis			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Alopecia			
subjects affected / exposed	3 / 238 (1.26%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	3	0	0
Dermatitis			

subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Dermatitis atopic			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Drug eruption			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Hand dermatitis			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Onychoclasis			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	0 / 238 (0.00%)	2 / 240 (0.83%)	0 / 218 (0.00%)
occurrences (all)	0	2	0
Rash			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Rash pustular			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Rash vesicular			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Skin lesion			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	1 / 218 (0.46%)
occurrences (all)	0	1	1
Solar dermatitis			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Urticaria			

subjects affected / exposed	0 / 238 (0.00%)	2 / 240 (0.83%)	0 / 218 (0.00%)
occurrences (all)	0	3	0
Rash pruritic			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Chronic kidney disease			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Haematuria			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Hypertonic bladder			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Leukocyturia			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Nephrolithiasis			
subjects affected / exposed	0 / 238 (0.00%)	2 / 240 (0.83%)	0 / 218 (0.00%)
occurrences (all)	0	2	0
Renal cyst			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Ureterolithiasis			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Urinary incontinence			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Goitre			

subjects affected / exposed	0 / 238 (0.00%)	3 / 240 (1.25%)	0 / 218 (0.00%)
occurrences (all)	0	3	0
Hyperparathyroidism			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Hypothyroidism			
subjects affected / exposed	1 / 238 (0.42%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	1	1	0
Thyroid mass			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	9 / 238 (3.78%)	13 / 240 (5.42%)	1 / 218 (0.46%)
occurrences (all)	11	15	1
Back pain			
subjects affected / exposed	9 / 238 (3.78%)	6 / 240 (2.50%)	3 / 218 (1.38%)
occurrences (all)	9	6	3
Bone pain			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Groin pain			
subjects affected / exposed	1 / 238 (0.42%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	1	1	0
Intervertebral disc disorder			
subjects affected / exposed	2 / 238 (0.84%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	2	0	0
Metatarsalgia			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	4 / 238 (1.68%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	4	2	0
Musculoskeletal disorder			

subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal pain			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	1 / 238 (0.42%)	4 / 240 (1.67%)	1 / 218 (0.46%)
occurrences (all)	1	4	1
Osteoarthritis			
subjects affected / exposed	9 / 238 (3.78%)	4 / 240 (1.67%)	3 / 218 (1.38%)
occurrences (all)	10	4	3
Pain in extremity			
subjects affected / exposed	5 / 238 (2.10%)	3 / 240 (1.25%)	1 / 218 (0.46%)
occurrences (all)	6	3	1
Spinal osteoarthritis			
subjects affected / exposed	4 / 238 (1.68%)	5 / 240 (2.08%)	0 / 218 (0.00%)
occurrences (all)	4	5	0
Spinal pain			
subjects affected / exposed	3 / 238 (1.26%)	2 / 240 (0.83%)	1 / 218 (0.46%)
occurrences (all)	3	2	1
Trigger finger			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Intervertebral disc degeneration			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	0	0	0
Myofascial pain syndrome			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Anal fungal infection			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	6 / 238 (2.52%)	5 / 240 (2.08%)	1 / 218 (0.46%)
occurrences (all)	7	5	1

Bronchitis bacterial			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
COVID 19			
subjects affected / exposed	9 / 238 (3.78%)	8 / 240 (3.33%)	2 / 218 (0.92%)
occurrences (all)	9	8	2
Chronic sinusitis			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Conjuctivitis			
subjects affected / exposed	1 / 238 (0.42%)	2 / 240 (0.83%)	0 / 218 (0.00%)
occurrences (all)	1	2	0
Cystitis			
subjects affected / exposed	3 / 238 (1.26%)	6 / 240 (2.50%)	1 / 218 (0.46%)
occurrences (all)	3	6	1
Diverticulitis			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	2	0	0
Gastrointestinal viral infection			
subjects affected / exposed	1 / 238 (0.42%)	4 / 240 (1.67%)	0 / 218 (0.00%)
occurrences (all)	1	4	0
Gastroenteritis			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Helicobacter infection			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Herpes virus infection			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Herpes zoster			
subjects affected / exposed	1 / 238 (0.42%)	1 / 240 (0.42%)	1 / 218 (0.46%)
occurrences (all)	1	1	1
Herpes zoster infection neurological			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0

Influenza			
subjects affected / exposed	3 / 238 (1.26%)	3 / 240 (1.25%)	0 / 218 (0.00%)
occurrences (all)	3	3	0
Laryngitis			
subjects affected / exposed	5 / 238 (2.10%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	5	1	0
Laryngopharyngitis			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Lower respiratory tract infection			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Mastitis			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	12 / 238 (5.04%)	7 / 240 (2.92%)	3 / 218 (1.38%)
occurrences (all)	14	7	3
Oral candidiasis			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Oral fungal infection			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Oral herpes			
subjects affected / exposed	1 / 238 (0.42%)	2 / 240 (0.83%)	0 / 218 (0.00%)
occurrences (all)	1	2	0
Periodontitis			
subjects affected / exposed	1 / 238 (0.42%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	1	1	0
Pharyngitis			
subjects affected / exposed	6 / 238 (2.52%)	2 / 240 (0.83%)	2 / 218 (0.92%)
occurrences (all)	8	2	2
Post-acute COVID-19 syndrome			
subjects affected / exposed	2 / 238 (0.84%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	2	0	0

Pulpitis dental			
subjects affected / exposed	0 / 238 (0.00%)	2 / 240 (0.83%)	0 / 218 (0.00%)
occurrences (all)	0	3	0
Respiratory tract infection			
subjects affected / exposed	3 / 238 (1.26%)	2 / 240 (0.83%)	2 / 218 (0.92%)
occurrences (all)	3	2	2
Sinusitis			
subjects affected / exposed	0 / 238 (0.00%)	5 / 240 (2.08%)	0 / 218 (0.00%)
occurrences (all)	0	5	0
Staphylococcal sepsis			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Tinea capitis			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Tinea versicolour			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Tonsillitis			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	17 / 238 (7.14%)	22 / 240 (9.17%)	3 / 218 (1.38%)
occurrences (all)	20	24	3
Upper respiratory tract infection bacterial			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	12 / 238 (5.04%)	10 / 240 (4.17%)	3 / 218 (1.38%)
occurrences (all)	12	10	3
Urinary tract infection bacterial			
subjects affected / exposed	3 / 238 (1.26%)	0 / 240 (0.00%)	2 / 218 (0.92%)
occurrences (all)	3	0	2
Urosepsis			

subjects affected / exposed	2 / 238 (0.84%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	2	0	0
Vestibular neuronitis			
subjects affected / exposed	2 / 238 (0.84%)	0 / 240 (0.00%)	2 / 218 (0.92%)
occurrences (all)	2	0	2
Viral abdominal infection			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Viral tracheitis			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 238 (0.42%)	3 / 240 (1.25%)	0 / 218 (0.00%)
occurrences (all)	1	3	0
Acarodermatitis			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences (all)	0	0	1
Acute sinusitis			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences (all)	0	0	1
Cervicitis human papilloma virus			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	0	0	0
Helicobacter gastritis			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	0	0	0
Otitis externa			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences (all)	0	0	1
Pharyngitis streptococcal			
subjects affected / exposed	0 / 238 (0.00%)	2 / 240 (0.83%)	0 / 218 (0.00%)
occurrences (all)	0	2	0
Respiratory tract infection viral			

subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	1 / 218 (0.46%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Glucose tolerance impaired			
subjects affected / exposed	0 / 238 (0.00%)	3 / 240 (1.25%)	0 / 218 (0.00%)
occurrences (all)	0	3	0
Hypercalcaemia			
subjects affected / exposed	2 / 238 (0.84%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	2	1	0
Hypercholesterolaemia			
subjects affected / exposed	6 / 238 (2.52%)	12 / 240 (5.00%)	1 / 218 (0.46%)
occurrences (all)	6	12	1
Hyperglycaemia			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Hyperlipidaemia			
subjects affected / exposed	1 / 238 (0.42%)	4 / 240 (1.67%)	0 / 218 (0.00%)
occurrences (all)	1	4	0
Hypertriglyceridaemia			
subjects affected / exposed	1 / 238 (0.42%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	1	0	0
Hypocalcaemia			
subjects affected / exposed	1 / 238 (0.42%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	1	1	0
Hypoglycaemia			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Impaired fasting glucose			
subjects affected / exposed	1 / 238 (0.42%)	2 / 240 (0.83%)	0 / 218 (0.00%)
occurrences (all)	1	2	0
Postprandial hypoglycaemia			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0

Purine metabolism disorder			
subjects affected / exposed	0 / 238 (0.00%)	1 / 240 (0.42%)	0 / 218 (0.00%)
occurrences (all)	0	1	0
Type 2 diabetes mellitus			
subjects affected / exposed	2 / 238 (0.84%)	3 / 240 (1.25%)	0 / 218 (0.00%)
occurrences (all)	2	3	0
Dehydration			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	0 / 238 (0.00%)	0 / 240 (0.00%)	0 / 218 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part 2 - Prolia-Bmab 1000	Part 2 - Prolia-Prolia	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 104 (27.88%)	27 / 104 (25.96%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign breast neoplasm			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Benign neoplasm of thyroid gland			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Breast cancer			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Clear cell renal cell carcinoma			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Colon cancer			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Haemangioma of liver			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Pancreatic carcinoma			

subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Papillary cystadenoma lymphomatosum			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Uterine leiomyoma			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 104 (0.00%)	1 / 104 (0.96%)	
occurrences (all)	0	1	
Vascular disorders			
Aortic arteriosclerosis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Essential hypertension			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Hypertension			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Peripheral venous disease			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Phlebitis superficial			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Thrombosis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Chest pain			

subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Exercise tolerance decreased			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Fatigue			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Injection site erythema			
subjects affected / exposed	0 / 104 (0.00%)	1 / 104 (0.96%)	
occurrences (all)	0	1	
Injection site pain			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Injection site swelling			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Peripheral swelling			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Pyrexia			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			
Endometrial hyperplasia			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Genital haemorrhage			

subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Ovarian cyst			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Uterine polyp			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Uterine prolapse			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Vulvovaginal pain			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Allergic sinusitis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Cough			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Epistaxis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Paranasal sinus inflammation			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Pulmonary fibrosis			

subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Pulmonary mass			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Reflux laryngitis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Rhinitis allergic			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract inflammation			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Sinus disorder			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Dyspnoea			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Anxiety disorder			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Depression			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Insomnia			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Schizophrenia			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Sleep disorder			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	

Investigations			
Adjusted calcium decreased			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Blood calcium decreased			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Blood calcium increased			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Blood cholesterol increased			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Blood parathyroid hormone increased			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Blood pressure increased			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Blood urine present			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	

Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Hepatic enzyme increased			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Low density lipoprotein increased			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Weight increased			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Amylase increased			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Blood glucose abnormal			
subjects affected / exposed	1 / 104 (0.96%)	0 / 104 (0.00%)	
occurrences (all)	1	0	
Blood parathyroid hormone decreased			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Weight decreased			
subjects affected / exposed	0 / 104 (0.00%)	1 / 104 (0.96%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Contusion			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Fascial rupture			

subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Foot fracture			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Hand fracture			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Head injury			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Immunisation reaction			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Incision site pain			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Ligament sprain			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Limb injury			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Lumbar vertebral fracture			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Meniscus injury			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Patella fracture			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Procedural pain			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Thoracic vertebral fracture			

subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Tooth fracture			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Arterial injury			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Epicondylitis			
subjects affected / exposed	1 / 104 (0.96%)	0 / 104 (0.00%)	
occurrences (all)	1	0	
Joint injury			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Radius fracture			
subjects affected / exposed	1 / 104 (0.96%)	0 / 104 (0.00%)	
occurrences (all)	1	0	
Skin laceration			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Spinal compression fracture			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Tendon rupture			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Forearm fracture			
subjects affected / exposed	0 / 104 (0.00%)	1 / 104 (0.96%)	
occurrences (all)	0	1	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	

Coronary artery disease			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Mitral valve incompetence			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Myocardial infarction			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Pulmonary valve incompetence			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Tricuspid valve incompetence			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Atrial fibrillation			
subjects affected / exposed	0 / 104 (0.00%)	1 / 104 (0.96%)	
occurrences (all)	0	1	
Nervous system disorders			
Carpal tunnel syndrome			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Cerebrovascular accident			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Dementia Alzheimer's type			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Dizziness			
subjects affected / exposed	1 / 104 (0.96%)	0 / 104 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	1 / 104 (0.96%)	0 / 104 (0.00%)	
occurrences (all)	1	0	
Hypoaesthesia			

subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Memory impairment			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Migraine			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Muscle contractions involuntary			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Neuralgia			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Neuropathy peripheral			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Sciatica			
subjects affected / exposed	0 / 104 (0.00%)	1 / 104 (0.96%)	
occurrences (all)	0	1	
Syncope			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Sinus headache			
subjects affected / exposed	0 / 104 (0.00%)	1 / 104 (0.96%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 104 (0.00%)	1 / 104 (0.96%)	
occurrences (all)	0	1	
Leukopenia			
subjects affected / exposed	1 / 104 (0.96%)	0 / 104 (0.00%)	
occurrences (all)	1	0	
Lymphadenitis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	

Macrocytosis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Neutropenia			
subjects affected / exposed	1 / 104 (0.96%)	0 / 104 (0.00%)	
occurrences (all)	1	0	
Thrombocytopenia			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Anaemia			
subjects affected / exposed	0 / 104 (0.00%)	1 / 104 (0.96%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Deafness unilateral			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Ear inflammation			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Noninfective mastoiditis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Tinnitus			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Ear pruritus			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Ear pain			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Cataract			
subjects affected / exposed	1 / 104 (0.96%)	0 / 104 (0.00%)	
occurrences (all)	1	0	
Eye pain			

subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Retinal tear			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Retinoschisis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Eye haemorrhage			
subjects affected / exposed	0 / 104 (0.00%)	1 / 104 (0.96%)	
occurrences (all)	0	1	
Conjunctivitis allergic			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 104 (0.96%)	0 / 104 (0.00%)	
occurrences (all)	1	0	
Abdominal pain upper			
subjects affected / exposed	1 / 104 (0.96%)	0 / 104 (0.00%)	
occurrences (all)	1	0	
Angular cheilitis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Barrett's oesophagus			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Chronic gastritis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Constipation			
subjects affected / exposed	0 / 104 (0.00%)	1 / 104 (0.96%)	
occurrences (all)	0	1	
Dental caries			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	

Diarrhoea			
subjects affected / exposed	1 / 104 (0.96%)	0 / 104 (0.00%)	
occurrences (all)	1	0	
Diverticulum intestinal			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Dyspepsia			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Food poisoning			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Gastric polyps			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Gastritis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorder			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Gingival pain			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Haemorrhoids			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Inflammatory bowel disease			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Oesophageal perforation			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	

Vomiting			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Gastric ulcer			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Hyperaesthesia teeth			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Large intestine polyp			
subjects affected / exposed	1 / 104 (0.96%)	0 / 104 (0.00%)	
occurrences (all)	1	0	
Mesenteric cyst			
subjects affected / exposed	0 / 104 (0.00%)	1 / 104 (0.96%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Oesophageal ulcer			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Reflux gastritis			
subjects affected / exposed	0 / 104 (0.00%)	1 / 104 (0.96%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Hepatic cyst			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Hepatic steatosis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Cholecystitis			

subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Actinic keratosis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Alopecia			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Dermatitis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Dermatitis atopic			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Drug eruption			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Erythema			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Hand dermatitis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Onychoclasis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Pruritus			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Rash			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	

Rash pustular			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Rash vesicular			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Skin lesion			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Solar dermatitis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Urticaria			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Rash pruritic			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Chronic kidney disease			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Haematuria			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Hypertonic bladder			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Leukocyturia			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Nephrolithiasis			

subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Renal cyst			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Ureterolithiasis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Urinary incontinence			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Hyperparathyroidism			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Hypothyroidism			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Thyroid mass			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 104 (0.00%)	2 / 104 (1.92%)	
occurrences (all)	0	2	
Back pain			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Bone pain			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Groin pain			

subjects affected / exposed	0 / 104 (0.00%)	1 / 104 (0.96%)	
occurrences (all)	0	1	
Intervertebral disc disorder			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Metatarsalgia			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Muscle spasms			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal disorder			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal pain			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Myalgia			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Osteoarthritis			
subjects affected / exposed	1 / 104 (0.96%)	0 / 104 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	1 / 104 (0.96%)	0 / 104 (0.00%)	
occurrences (all)	1	0	
Spinal osteoarthritis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Spinal pain			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Trigger finger			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Intervertebral disc degeneration			

subjects affected / exposed	0 / 104 (0.00%)	1 / 104 (0.96%)	
occurrences (all)	0	1	
Myofascial pain syndrome			
subjects affected / exposed	0 / 104 (0.00%)	1 / 104 (0.96%)	
occurrences (all)	0	1	
Infections and infestations			
Anal fungal infection			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Bronchitis			
subjects affected / exposed	1 / 104 (0.96%)	1 / 104 (0.96%)	
occurrences (all)	1	1	
Bronchitis bacterial			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
COVID 19			
subjects affected / exposed	2 / 104 (1.92%)	3 / 104 (2.88%)	
occurrences (all)	2	3	
Chronic sinusitis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Conjuctivitis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Cystitis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Diverticulitis			
subjects affected / exposed	1 / 104 (0.96%)	0 / 104 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal viral infection			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Gastroenteritis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	

Helicobacter infection			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Herpes virus infection			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Herpes zoster			
subjects affected / exposed	0 / 104 (0.00%)	1 / 104 (0.96%)	
occurrences (all)	0	1	
Herpes zoster infection neurological			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Influenza			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Laryngitis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Laryngopharyngitis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Mastitis			
subjects affected / exposed	0 / 104 (0.00%)	1 / 104 (0.96%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	4 / 104 (3.85%)	3 / 104 (2.88%)	
occurrences (all)	5	3	
Oral candidiasis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Oral fungal infection			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	

Oral herpes			
subjects affected / exposed	0 / 104 (0.00%)	1 / 104 (0.96%)	
occurrences (all)	0	1	
Periodontitis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Pharyngitis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Post-acute COVID-19 syndrome			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Pulpitis dental			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Respiratory tract infection			
subjects affected / exposed	1 / 104 (0.96%)	1 / 104 (0.96%)	
occurrences (all)	1	1	
Sinusitis			
subjects affected / exposed	1 / 104 (0.96%)	3 / 104 (2.88%)	
occurrences (all)	1	3	
Staphylococcal sepsis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Tinea capitis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Tinea versicolour			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Tonsillitis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	5 / 104 (4.81%)	3 / 104 (2.88%)	
occurrences (all)	5	3	

Upper respiratory tract infection bacterial				
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)		
occurrences (all)	0	0		
Urinary tract infection				
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)		
occurrences (all)	0	0		
Urinary tract infection bacterial				
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)		
occurrences (all)	0	0		
Urosepsis				
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)		
occurrences (all)	0	0		
Vestibular neuronitis				
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)		
occurrences (all)	0	0		
Viral abdominal infection				
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)		
occurrences (all)	0	0		
Viral tracheitis				
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)		
occurrences (all)	0	0		
Viral upper respiratory tract infection				
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)		
occurrences (all)	0	0		
Acarodermatitis				
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)		
occurrences (all)	0	0		
Acute sinusitis				
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)		
occurrences (all)	0	0		
Cervicitis human papilloma virus				
subjects affected / exposed	1 / 104 (0.96%)	0 / 104 (0.00%)		
occurrences (all)	1	0		
Conjunctivitis				

subjects affected / exposed	1 / 104 (0.96%)	0 / 104 (0.00%)	
occurrences (all)	1	0	
Helicobacter gastritis			
subjects affected / exposed	1 / 104 (0.96%)	0 / 104 (0.00%)	
occurrences (all)	1	0	
Otitis externa			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Pharyngitis streptococcal			
subjects affected / exposed	1 / 104 (0.96%)	0 / 104 (0.00%)	
occurrences (all)	1	0	
Respiratory tract infection viral			
subjects affected / exposed	0 / 104 (0.00%)	1 / 104 (0.96%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Glucose tolerance impaired			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Hypercalcaemia			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Hypercholesterolaemia			
subjects affected / exposed	1 / 104 (0.96%)	1 / 104 (0.96%)	
occurrences (all)	1	1	
Hyperglycaemia			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Hyperlipidaemia			
subjects affected / exposed	1 / 104 (0.96%)	0 / 104 (0.00%)	
occurrences (all)	1	0	
Hypertriglyceridaemia			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	

Hypocalcaemia			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Hypoglycaemia			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Impaired fasting glucose			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Postprandial hypoglycaemia			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Purine metabolism disorder			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 104 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	
Dehydration			
subjects affected / exposed	1 / 104 (0.96%)	0 / 104 (0.00%)	
occurrences (all)	1	0	
Gout			
subjects affected / exposed	0 / 104 (0.00%)	1 / 104 (0.96%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 January 2022	Original protocol, dated 06 Jan 2022
13 April 2022	Protocol Amendment 1, dated 13 Apr 2022 • Clarified that, for EMA, the PD endpoint AUEC of sCTX from baseline to 26 weeks was considered as Co-primary endpoint, while, for US FDA, this endpoint was considered as a secondary endpoint. • Changes to estimand labels with EMA and US FDA descriptors to add clarity on the purpose of each: Estimands 1a, 2, and 1b changed to 1a-EMA (Co-primary Efficacy), 1a-US FDA (Efficacy), and 1b-EMA (Co-primary PD), respectively. • Efficacy objective stated as primary for US FDA submission whilst efficacy and PD objectives are Co-primary for EMA. Furthermore, Estimand 1a-US FDA now uses the treatment policy strategy for discontinuation from treatment for any reason. • Specified that an ISRC was to be used for review of safety data to decide whether to pause/continue/modify the study. • Clarified that anti-resorptive therapy was to be provided to patients after the end-of-study or treatment discontinuation. • Clarified that any fracture was to be recorded as an AE/SAE/AESI (as applicable). • Added the details about the assessment and reporting of PFS related issues/AEs. • Clarified that Estimand 1a-US FDA now uses the treatment policy strategy for discontinuation from treatment for any reason. • Clarified which analysis sets were to be used for Estimand 1a-US FDA, Estimand 1a-EMA (Co-primary efficacy), and Estimand 1b-EMA (Co-primary PD) analyses. • Removed mFAS2 so that FAS was to be used instead for estimation of Estimand 1a-US FDA. Renamed mFAS1 as mFAS. Both 90% and 95% CIs were to be presented for primary efficacy. • Added that 95% CIs would be presented for the analyses of BMD after transition. • To address the US FDA recommendation to include an assessment of PFS related AEs, a footnote was added to schedule of events table to clarify about collection of PFS related issues.

31 August 2022	Protocol Amendment 2, dated 31 Aug 2022 • Added a Week 23 (Day 162) visit in Double-Blind Active-Controlled Period (Part 1) for blood sample collection for PD testing and other relevant assessments including PK. • Clarified that the use of COVID-19 vaccine was encouraged, although, at the discretion of the principal investigator, an interval of 7 days was advised between the COVID-19 vaccine and study drug administration due to putative adverse drug reactions. • Clarified that AE does not include pre-existing diseases or conditions present or detected prior to signing the ICF that does not worsen. • Deleted the following text "only if urinalysis dipstick results are abnormal" from clinical safety laboratory assessments. • Clarified that significant findings and illnesses to be reported after signing the ICF. • Updated the text for the sensitivity analysis of Estimand 1a-EMA (co-primary efficacy) to reflect missing data imputed under MI MAR approach, penalties and Rubin's method used for results. • Removed sensitivity analysis for Estimand 1a-US FDA as it was not required since sensitivity included in other estimands that were explored. • Added missing data imputed under MI MAR approach, penalties to reflect non-inferiority and non-superiority nulls, and results pooled using Rubin's method and 2 one-sided tests. • Clarified that Estimand 1a-US FDA (Efficacy) was to be performed but without the penalty being applied. • The occurrence and time to ICEs was to be considered and compared for the treatment groups. • Added a footnote to clarify that follicle-stimulating hormone was not required for women with surgical menopause as their postmenopausal status was to be confirmed via their medical history

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None reported.

Notes: