



Clinical trial results:

A Phase III, Randomised, Double-blind, Multicentre Clinical Study to Compare the Efficacy, Safety, Pharmacokinetics, Pharmacodynamics, and Immunogenicity between SB16 (proposed denosumab biosimilar) and Prolia® in Postmenopausal Women with Osteoporosis

Summary

EudraCT number	2020-001479-34
Trial protocol	LT DK CZ
Global end of trial date	03 January 2023

Results information

Result version number	v1 (current)
This version publication date	13 November 2024
First version publication date	13 November 2024

Trial information

Trial identification

Sponsor protocol code	SB16-3001
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Samsung Bioepis Co., Ltd.
Sponsor organisation address	76, Songdogoyoyuk-ro, Yeonsu-gu, Incheon, Korea, Republic of, 21987
Public contact	Information Desk, Samsung Bioepis Co., Ltd., +82 327280114, bioepisinfo@samsung.com
Scientific contact	Information Desk, Samsung Bioepis Co., Ltd., +82 327280114, bioepisinfo@samsung.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	03 January 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 January 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the equivalence of SB16 to Prolia®, in terms of percent change from baseline in lumbar spine bone mineral density (BMD) at Month 12 in subjects with postmenopausal osteoporosis (PMO).

Protection of trial subjects:

IPs were administered as a single subcutaneous injection in the upper arm, the upper thigh, or the abdomen. Only the Investigator or trained designee with an appropriate qualification (per local regulation) could perform and monitor the administration of IPs. In this study, IPs were administered only on an on-site basis.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 November 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 262
Country: Number of subjects enrolled	Czechia: 118
Country: Number of subjects enrolled	Denmark: 11
Country: Number of subjects enrolled	Lithuania: 25
Country: Number of subjects enrolled	Korea, Republic of: 41
Worldwide total number of subjects	457
EEA total number of subjects	416

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)	184
From 65 to 84 years	273
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at a total of 40 study centres: 9 centres in Czech Republic, 4 centres in Denmark, 4 centres in Lithuania, 13 centres in Poland, and 10 centres in Republic of Korea.

Pre-assignment

Screening details:

Subjects were randomised in a 1:1 ratio to receive either SB16 or Prolia subcutaneously at Months 0 and 6.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
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Arm title	SB16
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Arm description:

Subjects were randomly assigned to receive SB16 subcutaneously 60 mg at Months 0 and 6.

Arm type	Experimental
Investigational medicinal product name	SB16
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Solution for injection

Dosage and administration details:

60 mg every 6 months, Subcutaneous injection

Arm title	Prolia
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Arm description:

Subjects were randomly assigned to receive Prolia subcutaneously 60 mg at Months 0 and 6.

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

Dosage and administration details:

60 mg every 6 months, Subcutaneous injection

Number of subjects in period 1	SB16	Prolia
Started	225	232
Completed	206	201
Not completed	19	31
Consent withdrawn by subject	10	19
Physician decision	1	-
Adverse event, non-fatal	4	8
Other	-	1
Lack of efficacy	4	1
Protocol deviation	-	2

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	SB16+SB16

Arm description:

Subjects were randomly assigned to receive SB16 subcutaneously 60 mg at Months 0 and 6. At Month 12, subjects who received SB16 in the Main period continued to receive SB16, but they also followed the randomisation procedure to maintain blinding.

Arm type	Experimental
Investigational medicinal product name	SB16
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Solution for injection

Dosage and administration details:

60 mg every 6 months, Subcutaneous injection

Arm title	Prolia+SB16
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Arm description:

Subjects were randomly assigned to receive Prolia subcutaneously 60 mg at Months 0 and 6. At Month 12, subjects who received Prolia in the Main period of the SB16-3001 study were randomised again in a 1:1 ratio to either continue on Prolia (Prolia+Prolia) or were transitioned to SB16 (Prolia+SB16).

Arm type	Active comparator
Investigational medicinal product name	SB16
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Solution for injection

Dosage and administration details:
60 mg every 6 months, Subcutaneous injection

Arm title	Prolia+Prolia
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Arm description:

Subjects were randomly assigned to receive Prolia subcutaneously 60 mg at Months 0 and 6. At Month 12, subjects who received Prolia in the Main period of the SB16-3001 study were randomised again in a 1:1 ratio to either continue on Prolia (Prolia+Prolia) or were transitioned to SB16 (Prolia+SB16).

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

Dosage and administration details:
60 mg every 6 months, Subcutaneous injection

Number of subjects in period 2	SB16+SB16	Prolia+SB16	Prolia+Prolia
Started	206	100	101
Completed	206	99	99
Not completed	0	1	2
Consent withdrawn by subject	-	1	2

Baseline characteristics

Reporting groups

Reporting group title	SB16
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Reporting group description:

Subjects were randomly assigned to receive SB16 subcutaneously 60 mg at Months 0 and 6.

Reporting group title	Prolia
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Reporting group description:

Subjects were randomly assigned to receive Prolia subcutaneously 60 mg at Months 0 and 6.

Reporting group values	SB16	Prolia	Total
Number of subjects	225	232	457
Age categorical			
Units: Subjects			
Adults (18-64 years)	89	95	184
From 65-84 years	136	137	273
Age continuous			
Units: years			
arithmetic mean	66.5	66.3	
standard deviation	± 5.87	± 6.03	-
Gender categorical			
Units: Subjects			
Female	225	232	457
Male	0	0	0

End points

End points reporting groups

Reporting group title	SB16
Reporting group description: Subjects were randomly assigned to receive SB16 subcutaneously 60 mg at Months 0 and 6.	
Reporting group title	Prolia
Reporting group description: Subjects were randomly assigned to receive Prolia subcutaneously 60 mg at Months 0 and 6.	
Reporting group title	SB16+SB16
Reporting group description: Subjects were randomly assigned to receive SB16 subcutaneously 60 mg at Months 0 and 6. At Month 12, subjects who received SB16 in the Main period continued to receive SB16, but they also followed the randomisation procedure to maintain blinding.	
Reporting group title	Prolia+SB16
Reporting group description: Subjects were randomly assigned to receive Prolia subcutaneously 60 mg at Months 0 and 6. At Month 12, subjects who received Prolia in the Main period of the SB16-3001 study were randomised again in a 1:1 ratio to either continue on Prolia (Prolia+Prolia) or were transitioned to SB16 (Prolia+SB16).	
Reporting group title	Prolia+Prolia
Reporting group description: Subjects were randomly assigned to receive Prolia subcutaneously 60 mg at Months 0 and 6. At Month 12, subjects who received Prolia in the Main period of the SB16-3001 study were randomised again in a 1:1 ratio to either continue on Prolia (Prolia+Prolia) or were transitioned to SB16 (Prolia+SB16).	

Primary: Percent Change from Baseline in Lumbar Spine BMD at Month 12

End point title	Percent Change from Baseline in Lumbar Spine BMD at Month 12
End point description:	
End point type	Primary
End point timeframe: At Month 12	

End point values	SB16	Prolia		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	225	231		
Units: Percent Change from Baseline				
least squares mean (standard error)	5.63 (± 0.250)	5.30 (± 0.254)		

Statistical analyses

Statistical analysis title	Equivalence test
Comparison groups	SB16 v Prolia
Number of subjects included in analysis	456
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Least squares mean difference
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.36
upper limit	1.03

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were collected from the time of signing the written informed consent until the EOS/ET.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.0
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Reporting groups

Reporting group title	SB16
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Reporting group description:

Subjects were randomly assigned to receive SB16 subcutaneously 60 mg at Months 0 and 6. At Month 12, subjects who received SB16 in the Main period continued to receive SB16, but they also followed the randomisation procedure to maintain blinding.

Reporting group title	Prolia+SB16/Prolia+Prolia
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Reporting group description:

Subjects were randomly assigned to receive Prolia subcutaneously 60 mg at Months 0 and 6. At Month 12, subjects who received Prolia in the Main period of the SB16-3001 study were randomised again in a 1:1 ratio to either continue on Prolia (Prolia+Prolia) or were transitioned to SB16 (Prolia+SB16).

Reporting group title	Prolia+SB16
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Reporting group description:

Subjects were randomly assigned to receive Prolia subcutaneously 60 mg at Months 0 and 6. At Month 12, subjects who received Prolia in the Main period of the SB16-3001 study were randomised again in a 1:1 ratio to either continue on Prolia (Prolia+Prolia) or were transitioned to SB16 (Prolia+SB16).

Reporting group title	Prolia+Prolia
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Reporting group description: -

Serious adverse events	SB16	Prolia+SB16/Prolia+Prolia	Prolia+SB16
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 225 (5.33%)	11 / 231 (4.76%)	5 / 100 (5.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adrenal adenoma			
subjects affected / exposed	1 / 225 (0.44%)	0 / 231 (0.00%)	0 / 100 (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
Breast cancer			
subjects affected / exposed	0 / 225 (0.00%)	1 / 231 (0.43%)	0 / 100 (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

Lung adenocarcinoma			
subjects affected / exposed	0 / 225 (0.00%)	1 / 231 (0.43%)	0 / 100 (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			
Forearm fracture			
subjects affected / exposed	2 / 225 (0.89%)	0 / 231 (0.00%)	0 / 100 (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
Ankle fracture			
subjects affected / exposed	1 / 225 (0.44%)	0 / 231 (0.00%)	0 / 100 (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
Femoral neck fracture			
subjects affected / exposed	1 / 225 (0.44%)	0 / 231 (0.00%)	0 / 100 (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
Subdural haemorrhage			
subjects affected / exposed	1 / 225 (0.44%)	0 / 231 (0.00%)	0 / 100 (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
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 225 (0.00%)	1 / 231 (0.43%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Intracranial aneurysm			
subjects affected / exposed	1 / 225 (0.44%)	0 / 231 (0.00%)	0 / 100 (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
Transient ischaemic attack			

subjects affected / exposed	0 / 225 (0.00%)	1 / 231 (0.43%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	0 / 225 (0.00%)	1 / 231 (0.43%)	0 / 100 (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
Eye disorders			
Cataract			
subjects affected / exposed	0 / 225 (0.00%)	1 / 231 (0.43%)	0 / 100 (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
Retinal detachment			
subjects affected / exposed	0 / 225 (0.00%)	1 / 231 (0.43%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Intestinal infarction			
subjects affected / exposed	1 / 225 (0.44%)	0 / 231 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 225 (0.44%)	0 / 231 (0.00%)	0 / 100 (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
Pulmonary embolism			
subjects affected / exposed	1 / 225 (0.44%)	0 / 231 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Haematuria			

subjects affected / exposed	0 / 225 (0.00%)	1 / 231 (0.43%)	0 / 100 (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
Nephrolithiasis			
subjects affected / exposed	0 / 225 (0.00%)	1 / 231 (0.43%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral caruncle			
subjects affected / exposed	0 / 225 (0.00%)	1 / 231 (0.43%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	1 / 225 (0.44%)	1 / 231 (0.43%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal osteoarthritis			
subjects affected / exposed	1 / 225 (0.44%)	0 / 231 (0.00%)	0 / 100 (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
Intervertebral disc disorder			
subjects affected / exposed	0 / 225 (0.00%)	1 / 231 (0.43%)	0 / 100 (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
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 225 (0.44%)	0 / 231 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 225 (0.44%)	0 / 231 (0.00%)	0 / 100 (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

Intervertebral discitis			
subjects affected / exposed	0 / 225 (0.00%)	1 / 231 (0.43%)	0 / 100 (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
Septic shock			
subjects affected / exposed	0 / 225 (0.00%)	1 / 231 (0.43%)	0 / 100 (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

Serious adverse events	Prolia+Prolia		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 101 (2.97%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adrenal adenoma			
subjects affected / exposed	0 / 101 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Breast cancer			
subjects affected / exposed	0 / 101 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung adenocarcinoma			
subjects affected / exposed	0 / 101 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Forearm fracture			
subjects affected / exposed	0 / 101 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ankle fracture			

subjects affected / exposed	0 / 101 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Femoral neck fracture			
subjects affected / exposed	0 / 101 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subdural haemorrhage			
subjects affected / exposed	0 / 101 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 101 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Intracranial aneurysm			
subjects affected / exposed	0 / 101 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	0 / 101 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Cataract			

subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Retinal detachment			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Intestinal infarction			
subjects affected / exposed	0 / 101 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 101 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	0 / 101 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 101 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nephrolithiasis			
subjects affected / exposed	0 / 101 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urethral caruncle			
subjects affected / exposed	0 / 101 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 101 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal osteoarthritis			
subjects affected / exposed	0 / 101 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc disorder			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 101 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 101 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intervertebral discitis			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	SB16	Prolia+SB16/Prolia+Prolia	Prolia+SB16
Total subjects affected by non-serious adverse events			
subjects affected / exposed	116 / 225 (51.56%)	107 / 231 (46.32%)	46 / 100 (46.00%)
Nervous system disorders			
Headache			
subjects affected / exposed	17 / 225 (7.56%)	13 / 231 (5.63%)	8 / 100 (8.00%)
occurrences (all)	21	15	9
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	21 / 225 (9.33%)	12 / 231 (5.19%)	7 / 100 (7.00%)
occurrences (all)	24	13	8
Osteoarthritis			
subjects affected / exposed	11 / 225 (4.89%)	11 / 231 (4.76%)	5 / 100 (5.00%)
occurrences (all)	12	13	5
Musculoskeletal pain			
subjects affected / exposed	4 / 225 (1.78%)	7 / 231 (3.03%)	6 / 100 (6.00%)
occurrences (all)	4	7	6
Infections and infestations			
COVID-19			
subjects affected / exposed	20 / 225 (8.89%)	18 / 231 (7.79%)	5 / 100 (5.00%)
occurrences (all)	20	18	5
Upper respiratory tract infection			
subjects affected / exposed	13 / 225 (5.78%)	12 / 231 (5.19%)	3 / 100 (3.00%)
occurrences (all)	17	12	3
Urinary tract infection			
subjects affected / exposed	13 / 225 (5.78%)	7 / 231 (3.03%)	1 / 100 (1.00%)
occurrences (all)	16	7	1
Nasopharyngitis			
subjects affected / exposed	10 / 225 (4.44%)	18 / 231 (7.79%)	7 / 100 (7.00%)
occurrences (all)	11	19	8
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	23 / 225 (10.22%)	27 / 231 (11.69%)	11 / 100 (11.00%)
occurrences (all)	26	29	12
Hypercholesterolaemia			

subjects affected / exposed	16 / 225 (7.11%)	7 / 231 (3.03%)	2 / 100 (2.00%)
occurrences (all)	16	7	2
Vitamin D deficiency			
subjects affected / exposed	11 / 225 (4.89%)	9 / 231 (3.90%)	6 / 100 (6.00%)
occurrences (all)	11	9	6

Non-serious adverse events	Prolia+Prolia		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 101 (48.51%)		
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 101 (4.95%)		
occurrences (all)	6		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 101 (3.96%)		
occurrences (all)	4		
Osteoarthritis			
subjects affected / exposed	6 / 101 (5.94%)		
occurrences (all)	8		
Musculoskeletal pain			
subjects affected / exposed	0 / 101 (0.00%)		
occurrences (all)	0		
Infections and infestations			
COVID-19			
subjects affected / exposed	11 / 101 (10.89%)		
occurrences (all)	11		
Upper respiratory tract infection			
subjects affected / exposed	5 / 101 (4.95%)		
occurrences (all)	5		
Urinary tract infection			
subjects affected / exposed	5 / 101 (4.95%)		
occurrences (all)	5		
Nasopharyngitis			
subjects affected / exposed	9 / 101 (8.91%)		
occurrences (all)	9		
Metabolism and nutrition disorders			

Hypocalcaemia			
subjects affected / exposed	13 / 101 (12.87%)		
occurrences (all)	14		
Hypercholesterolaemia			
subjects affected / exposed	5 / 101 (4.95%)		
occurrences (all)	5		
Vitamin D deficiency			
subjects affected / exposed	3 / 101 (2.97%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 May 2021	This amendment considered clarifications on: <ul style="list-style-type: none">•To add secondary objective considering percentage change from baseline in lumbar spine BMD at Month 6•To add AUEC0-M6 of serum CTX as a secondary endpoint•To add the additional information for missing data imputation

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported