Clinical trial results:
A Randomised, Double-blind, Multicentre Phase III Study to Assess the Efficacy and Safety of RGB-14-P Compared to Prolia® in Women with Postmenopausal Osteoporosis

Summary

EudraCT number	2020-006017-38
Trial protocol	PL CZ HU BG ES IT
Global end of trial date	15 November 2023

Results information

Result version number	v1 (current)
This version publication date	25 October 2024
First version publication date	25 October 2024

Trial information

Trial identification

Sponsor protocol code	RGB-14-101

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05087030
WHO universal trial number (UTN)	-
Other trial identifiers	IND: 146025

Notes:

Sponsors

Sponsor organisation name	Gedeon Richter Plc.
Sponsor organisation address	1103 Budapest, Gyömrői út 19-21, Budapest, Hungary,
Public contact	Medical Information Service, Gedeon Richter Plc., medinfo@richter.hu
Scientific contact	Medical Information Service, Gedeon Richter Plc., medinfo@richter.hu

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	13 February 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 November 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Efficacy
To demonstrate similar efficacy and effect of RGB 14 P with US licensed Prolia® on BMD at the lumbar spine at Week 52 in female subjects with postmenopausal osteoporosis

Pharmacodynamics
To demonstrate similar pharmacodynamics (AUEC of %CfB in sCTX) of RGB 14 P with US licensed Prolia® in female subjects with postmenopausal osteoporosis (only required for EMA)

Protection of trial subjects:

This study was conducted in accordance with the principles laid down in the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) guidance – ICH E6(R2), and in accordance with the Declaration of Helsinki and in accordance with applicable national laws and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 September 2021
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	Poland: 225
Country: Number of subjects enrolled	Spain: 35
Country: Number of subjects enrolled	Bulgaria: 67
Country: Number of subjects enrolled	Czechia: 61
Country: Number of subjects enrolled	Hungary: 39
Country: Number of subjects enrolled	Italy: 23
Country: Number of subjects enrolled	United States: 20
Country: Number of subjects enrolled	Ukraine: 3
Worldwide total number of subjects	473
EEA total number of subjects	450

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)	186
From 65 to 84 years	287
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted between 21-September-2021 (first subject first visit) to 15-November-2023 (last subject last visit).

Pre-assignment

Screening details:

Subjects who met the inclusion criteria and none of the exclusion criteria were enrolled to the study. All study assessments were performed as per the schedule of assessment.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	RGB-14-P

Arm description:

Subjects received RGB-14-P as subcutaneous (SC) injection on Day 1 of treatment period 1 (week 0) and treatment period 2 (week 26).

Arm type	Experimental
Investigational medicinal product name	RGB-14-P
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

RGB-14-P was provided as a single-dose (1 mL solution) pre-filled syringe for subcutaneous injection administration.

Arm title	Prolia®

Arm description:

Subjects received Prolia® as SC injection on Day 1 of treatment period 1 (week 0) and treatment period 2 (week 26).

Arm type	Experimental
Investigational medicinal product name	Prolia®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Prolia® was provided as a single-dose (1 mL solution) pre-filled syringe for subcutaneous injection administration.

Number of subjects in period 1	RGB-14-P	Prolia®
Started	242	231
Completed	225	211
Not completed	17	20
Exclusion criteria met	1	-
Adverse event, serious fatal	-	1
Consent withdrawn by subject	8	13
Adverse event, non-fatal	2	2
Unspecified	1	2
Lost to follow-up	3	-
Study objective confounded	1	-
Subject's personal reason	-	2
Protocol deviation	1	-

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

Arms

Are arms mutually exclusive?	Yes
Arm title	RGB-14-P to RGB-14-P

Arm description:

Subjects who received RGB-14-P during the main period were re-randomized and received Prolia® as SC injection on day 1 of treatment period 3 (week 52).

Arm type	Experimental
Investigational medicinal product name	RGB-14-P
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

RGB-14-P was provided as a single-dose (1 mL solution) pre-filled syringe for subcutaneous injection administration.

Arm title	Prolia® to RGB-14-P

Arm description:

Subjects who received Prolia® during the main period were re-randomized and received RGB-14-P as SC injection on Day 1 of treatment period 3 (week 52).

Arm type	Experimental

Investigational medicinal product name	Prolia®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Prolia® was provided as a single-dose (1 mL solution) pre-filled syringe for subcutaneous injection administration.

Arm title	Prolia® to Prolia®

Arm description:

Subjects who received Prolia® during the main period were re-randomized and received Prolia® as SC injection on Day 1 of treatment period 3 (week 52).

Arm type	Experimental
Investigational medicinal product name	Prolia®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Prolia® was provided as a single-dose (1 mL solution) pre-filled syringe for subcutaneous injection administration.

Number of subjects in period 2[1]	RGB-14-P to RGB-14-P	Prolia® to RGB-14-P	Prolia® to Prolia®
Started	63	62	63
Completed	63	62	62
Not completed	0	0	1
Consent withdrawn by subject	-	-	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Only a subset of patients continued the study in the Transition period (as outlined in the clinical study protocol).

Baseline characteristics

Reporting groups	
Reporting group title	RGB-14-P
Reporting group description:	
Subjects received RGB-14-P as subcutaneous (SC) injection on Day 1 of treatment period 1 (week 0) and treatment period 2 (week 26).	
Reporting group title	Prolia®
Reporting group description:	
Subjects received Prolia® as SC injection on Day 1 of treatment period 1 (week 0) and treatment period 2 (week 26).	

Reporting group values	RGB-14-P	Prolia®	Total
Number of subjects	242	231	473
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	100	86	186
From 65-84 years	142	145	287
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	66.7	66.8	
standard deviation	± 5.20	± 4.91	-
Gender categorical Units: Subjects			
Female	242	231	473
Male	0	0	0

End points

End points reporting groups

Reporting group title	RGB-14-P
Reporting group description:	
Subjects received RGB-14-P as subcutaneous (SC) injection on Day 1 of treatment period 1 (week 0) and treatment period 2 (week 26).	
Reporting group title	Prolia®
Reporting group description:	
Subjects received Prolia® as SC injection on Day 1 of treatment period 1 (week 0) and treatment period 2 (week 26).	
Reporting group title	RGB-14-P to RGB-14-P
Reporting group description:	
Subjects who received RGB-14-P during the main period were re-randomized and received Prolia® as SC injection on day 1 of treatment period 3 (week 52).	
Reporting group title	Prolia® to RGB-14-P
Reporting group description:	
Subjects who received Prolia® during the main period were re-randomized and received RGB-14-P as SC injection on Day 1 of treatment period 3 (week 52).	
Reporting group title	Prolia® to Prolia®
Reporting group description:	
Subjects who received Prolia® during the main period were re-randomized and received Prolia® as SC injection on Day 1 of treatment period 3 (week 52).	

Primary: Percentage Change from Baseline (%CfB) in Lumbar Spine Bone Mineral Density (BMD)

End point title	Percentage Change from Baseline (%CfB) in Lumbar Spine Bone Mineral Density (BMD)
End point description:	
Percentage change from baseline in lumbar bone BMD was assessed. BMD at the lumbar spine was measured by dual-energy x-ray absorptiometry (DXA). This outcome measure was assessed for main period. The Full analysis set (FAS) included all subjects to whom the investigational medicinal product (IMP) has been randomized. Here, 'number of subjects analyzed' specifies all subjects who were evaluated for this outcome measure.	
End point type	Primary
End point timeframe:	
Week 52	

End point values	RGB-14-P	Prolia®		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	222	206		
Units: percent				
arithmetic mean (standard deviation)	5.68 (± 3.535)	5.19 (± 4.118)		

Statistical analyses

Statistical analysis title	RGB-14-P v/s Prolia®

Statistical analysis description:

The analysis was performed with an ANCOVA model with %CfB in lumbar spine BMD at Week 52 as the dependent variable; covariates were treatment Arm (RGB-14-P and US licenced Prolia), stratification factors at randomization (Previous use of bisphosphonates [yes/no] and geographical region [Europe, US], Baseline BMD value in lumbar spine, machine type and machine type*baseline BMD value interaction.

Comparison groups	RGB-14-P v Prolia®
Number of subjects included in analysis	428
Analysis specification	Pre-specified
Analysis type	equivalence[1]
Parameter estimate	Estimated Difference
Point estimate	0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.402
upper limit	1.09

Notes:

[1] - Comparison between Study Treatment Groups

Primary: Area Under the Effective Curve (AUEC) After the First Dose Until Day 183 of %CfB in serum Type I Collagen C-telopeptide (sCTX)

End point title	Area Under the Effective Curve (AUEC) After the First Dose Until Day 183 of %CfB in serum Type I Collagen C-telopeptide (sCTX)

End point description:

The AUEC of %CfB in sCTX of RGB-14-P was assessed as part of pharmacodynamics parameter with US-licensed Prolia® in female subjects was demonstrated with postmenopausal osteoporosis. This outcome measure was assessed for main period only.
The pharmacodynamic analysis set (PDS) included all subjects in the safety population with at least one evaluable pharmacodynamic (PD) parameter (%CfB and AUEC) and not had any protocol deviations that have a relevant impact on sCTX or serum procollagen type 1 N-terminal propeptide (P1NP) results included in the pharmacodynamic parameter calculation. Here, 'number of subjects analyzed' specifies all subjects who were evaluated for this outcome measure.

End point type	Primary

End point timeframe:

Week 26

End point values	RGB-14-P	Prolia®		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	241	229		
Units: milligram(s)/deciliter(dL)*day				
geometric mean (confidence interval 95%)	13501.300 (12737.814 to 14264.794)	13344.650 (12583.291 to 14106.002)		

Statistical analyses

Statistical analysis title	RGB-14-P v/s Prolia®

Statistical analysis description:

The analysis was performed with a mixed-effects model ANCOVA on natural log-transformed AUEC data as the dependent variable and the following model covariates: Treatment Arm, Stratification factors (Previous use of bisphosphonates [yes/no] and Geographical region [Europe, US], Log of baseline sCTX.

Comparison groups	RGB-14-P v Prolia®
Number of subjects included in analysis	470
Analysis specification	Pre-specified
Analysis type	equivalence[2]
Parameter estimate	Geometric Mean Ratio
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.978
upper limit	1.046

Notes:

[2] - Comparison between Study Treatment Groups

Secondary: Percentage Change from Baseline (%CfB) in Total Hip BMD

End point title	Percentage Change from Baseline (%CfB) in Total Hip BMD

End point description:

Percentage Change from Baseline in total hip BMD was assessed.
The FAS included all subjects to whom the IMP has been randomized. Here, 'number of subjects analyzed' specifies all subjects who were evaluated for this outcome measure.
Here, 9999 indicates that the data were not available due to insufficient number of subjects.

End point type	Secondary

End point timeframe:

Weeks 26, 52 and 78

End point values	RGB-14-P	RGB-14-P to RGB-14-P	Prolia®	Prolia® to RGB-14-P
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	225	63	211	62
Units: percent				
arithmetic mean (standard deviation)				
Week 26 (n = 225, 62, 211, 58, 62)	2.42 (± 2.659)	2.46 (± 2.712)	2.69 (± 2.519)	2.81 (± 2.607)
Week 52 (n = 220, 63, 205, 60, 63)	3.42 (± 2.916)	3.03 (± 3.103)	3.49 (± 2.872)	3.36 (± 2.696)
Week 78 (n = 0, 62, 0, 62, 60)	9999 (± 9999)	4.24 (± 3.381)	9999 (± 9999)	4.12 (± 3.128)

End point values	Prolia® to Prolia®			
Subject group type	Reporting group			
Number of subjects analysed	63			
Units: percent				
arithmetic mean (standard deviation)				
Week 26 (n = 225, 62, 211, 58, 62)	3.35 (± 2.559)			

Week 52 (n = 220, 63, 205, 60, 63) Week 78 (n = 0, 62, 0, 62, 60)	4.21 (± 3.452) 4.95 (± 3.849)			

Statistical analyses

Statistical analysis title	RGB-14-P v/s Prolia® at Week 26
Statistical analysis description: at Week 26	
Comparison groups	RGB-14-P v Prolia®
Number of subjects included in analysis	436
Analysis specification	Pre-specified
Analysis type	other[3]
Parameter estimate	Estimated Difference
Point estimate	-0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.792
upper limit	0.165

Notes:

[3] - Mixed Model Repeated Measures

Statistical analysis title	RGB-14-P v/s Prolia® at Week 52
Statistical analysis description: at Week 52	
Comparison groups	RGB-14-P v Prolia®
Number of subjects included in analysis	436
Analysis specification	Pre-specified
Analysis type	other[4]
Parameter estimate	Estimated Difference
Point estimate	-0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.68
upper limit	0.358

Notes:

[4] - Mixed model repeated measures

Secondary: Percentage Change from Baseline (%CfB) in Lumbar Spine BMD

End point title	Percentage Change from Baseline (%CfB) in Lumbar Spine BMD

End point description:

Percentage Change from Baseline in lumbar spine BMD was assessed.
The Full analysis set (FAS) included all subjects to whom the IMP has been randomized. Here, 'number of subjects analyzed' specifies all subjects who were evaluated for this outcome measure.
Here, 9999 indicates that the data were not available due to insufficient number of subjects.

End point type	Secondary

End point timeframe:
Weeks 26 and 78

End point values	RGB-14-P	RGB-14-P to RGB-14-P	Prolia®	Prolia® to RGB-14-P
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	227	63	218	62
Units: percent				
arithmetic mean (standard deviation)				
Week 26 (n= 227, 62, 218, 61, 63)	3.56 (± 3.747)	3.98 (± 3.185)	3.45 (± 4.227)	3.39 (± 3.848)
Week 78 (n= 0, 63, 0, 62, 60)	9999 (± 9999)	7.03 (± 3.828)	9999 (± 9999)	7.06 (± 4.327)

End point values	Prolia® to Prolia®			
Subject group type	Reporting group			
Number of subjects analysed	63			
Units: percent				
arithmetic mean (standard deviation)				
Week 26 (n= 227, 62, 218, 61, 63)	3.68 (± 4.979)			
Week 78 (n= 0, 63, 0, 62, 60)	7.09 (± 4.240)			

Statistical analyses

Statistical analysis title	RGB-14-P v/s Prolia® at Week 26
Statistical analysis description: Week 26	
Comparison groups	RGB-14-P v Prolia®
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[5]
Parameter estimate	Estimated Difference
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.703
upper limit	0.769

Notes:
[5] - mixed model for repeated measures

Secondary: Percentage Change from Baseline (%CfB) in Femoral Neck BMD

End point title	Percentage Change from Baseline (%CfB) in Femoral Neck BMD

End point description:
Percentage Change from Baseline in femoral neck BMD was assessed by DXA.

The FAS included all subjects to whom the IMP has been randomized. Here, 'number of subjects analyzed' specifies all subjects who were evaluated for this outcome measure.
Here, 9999 indicates that the data were not available due to insufficient number of subjects.

End point type	Secondary

End point timeframe:

Weeks 26, 52 and 78

End point values	RGB-14-P	RGB-14-P to RGB-14-P	Prolia®	Prolia® to RGB-14-P
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	225	63	211	62
Units: percent				
arithmetic mean (standard deviation)				
Week 26 (n= 225, 62, 211, 58, 62)	1.88 (± 3.040)	1.60 (± 2.833)	1.94 (± 3.610)	2.21 (± 3.296)
Week 52 (n= 220, 63, 205, 60, 63)	2.42 (± 3.687)	1.95 (± 3.621)	2.64 (± 3.751)	2.60 (± 3.127)
Week 78 (n= 0, 63, 0, 62, 60)	9999 (± 9999)	3.08 (± 4.259)	9999 (± 9999)	3.06 (± 3.337)

End point values	Prolia® to Prolia®			
Subject group type	Reporting group			
Number of subjects analysed	63			
Units: percent				
arithmetic mean (standard deviation)				
Week 26 (n= 225, 62, 211, 58, 62)	2.35 (± 4.057)			
Week 52 (n= 220, 63, 205, 60, 63)	3.24 (± 4.549)			
Week 78 (n= 0, 63, 0, 62, 60)	4.04 (± 4.764)			

Statistical analyses

Statistical analysis title	RGB-14-P v/s Prolia® at Week 26

Statistical analysis description:

The analysis was performed with a mixed model repeated measures with observed %CfB in femoral neck BMD as the dependent variable; covariates were treatment arm (RGB-14-P and US licenced Prolia), stratification factors at randomization (Previous use of
bisphosphonates [yes/no] and geographical region [Europe, US], Baseline BMD value in femoral neck, machine type and machine
type*baseline BMD value interaction, study week and study week*treatment arm interaction.

Comparison groups	RGB-14-P v Prolia®
Number of subjects included in analysis	436
Analysis specification	Pre-specified
Analysis type	other[6]
Parameter estimate	Estimated Difference
Point estimate	-0.12

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.727
upper limit	0.478

Notes:

[6] - Mixed model repeated measures

Statistical analysis title	RGB-14-P v/s Prolia® at Week 52

Statistical analysis description:

The analysis was performed with a mixed model repeated measures with observed %CfB in femoral neck BMD as the dependent variable; covariates were treatment arm (RGB-14-P and US licenced Prolia), stratification factors at randomization (Previous use of
bisphosphonates [yes/no] and geographical region [Europe, US], Baseline BMD value in femoral neck, machine type and machine
type*baseline BMD value interaction, study week and study week*treatment arm interaction.

Comparison groups	RGB-14-P v Prolia®
Number of subjects included in analysis	436
Analysis specification	Pre-specified
Analysis type	other[7]
Parameter estimate	Estimated Difference
Point estimate	-0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.006
upper limit	0.359

Notes:

[7] - Mixed model repeated measures

Secondary: Number of Subjects with Vertebral Fragility Fracture

End point title	Number of Subjects with Vertebral Fragility Fracture

End point description:

Number of subjects with vertebral fragility fracture were assessed. Information on vertebral fractures was centrally collected through the evaluation of lateral thoraco-lumbar spine X-ray.
The Full analysis set (FAS) included all subjects to whom the IMP has been randomized. Here, 'number of subjects analyzed' specifies all subjects who were evaluated for this outcome measure.
Here, 9999 indicates that the data were not available due to insufficient number of subjects.

End point type	Secondary

End point timeframe:

Weeks 52 and 78

End point values	RGB-14-P	RGB-14-P to RGB-14-P	Prolia®	Prolia® to RGB-14-P
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	242	63	231	62
Units: Subjects				
Week 52 (n= 242, 0, 231, 0, 0)	4	9999	8	9999
Week 78 (n= 0, 63, 0, 62, 63)	9999	3	9999	4

End point values	Prolia® to Prolia®			
Subject group type	Reporting group			
Number of subjects analysed	63			
Units: Subjects				
Week 52 (n= 242, 0, 231, 0, 0)	9999			
Week 78 (n= 0, 63, 0, 62, 63)	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Non-Vertebral Fragility Fracture

End point title	Number of Subjects with Non-Vertebral Fragility Fracture

End point description:

Number of subjects with non-vertebral fragility fracture were assessed. Information on non-vertebral fractures was centrally collected through the evaluation of lateral thoraco-lumbar spine X-ray.
The FAS included all subjects to whom the IMP has been randomized. Here, 'number of subjects analyzed' specifies all subjects who were evaluated for this outcome measure.
Here, 9999 indicates that the data were not available due to insufficient number of subjects.

End point type	Secondary

End point timeframe:

Weeks 52 and 78

End point values	RGB-14-P	RGB-14-P to RGB-14-P	Prolia®	Prolia® to RGB-14-P
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	242	63	231	62
Units: Subjects				
Week 52 (n= 242, 0, 231, 0, 0)	4	9999	10	9999
Week 78 (n= 0, 63, 0, 62, 63)	9999	2	9999	5

End point values	Prolia® to Prolia®			
Subject group type	Reporting group			
Number of subjects analysed	63			
Units: Subjects				
Week 52 (n= 242, 0, 231, 0, 0)	9999			
Week 78 (n= 0, 63, 0, 62, 63)	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change from Baseline (%CfB) in Serum Procollagen Type 1 N Terminal Propeptide (P1NP)

End point title	Percentage Change from Baseline (%CfB) in Serum Procollagen Type 1 N Terminal Propeptide (P1NP)

End point description:

Percentage Change from Baseline in serum P1NP was assessed as part of pharmacodynamics parameter with US-licensed Prolia® in female subjects with postmenopausal osteoporosis.
The PDS included all subjects in safety population with at least one evaluable PD parameter (%CfB and AUEC) and not had any protocol deviations that have a relevant impact on sCTX or serum P1NP results included in PD parameter calculation. Here, 'number of subjects analyzed' specifies all subjects who were evaluated for this outcome measure.
Here, 9999 indicates that the data were not available due to insufficient number of subjects.

End point type	Secondary

End point timeframe:

Weeks 4, 26, 52 and 78

End point values	RGB-14-P	RGB-14-P to RGB-14-P	Prolia®	Prolia® to RGB-14-P
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	234	60	220	60
Units: percent				
arithmetic mean (standard deviation)				
Week 4 (n= 234, 60, 220, 59, 62)	22.10 (± 14.905)	19.85 (± 13.939)	20.22 (± 15.091)	18.45 (± 15.835)
Week 26 (n= 216, 57, 211, 59, 60)	65.92 (± 17.828)	68.42 (± 11.693)	62.89 (± 29.294)	63.41 (± 42.677)
Week 52 (n= 204, 60, 198, 60, 61)	65.04 (± 19.131)	64.86 (± 16.902)	63.82 (± 21.712)	66.05 (± 20.428)
Week 78 (n= 0, 54, 0, 59, 58)	9999 (± 9999)	64.12 (± 18.845)	9999 (± 9999)	66.91 (± 16.816)

End point values	Prolia® to Prolia®			
Subject group type	Reporting group			
Number of subjects analysed	62			
Units: percent				
arithmetic mean (standard deviation)				
Week 4 (n= 234, 60, 220, 59, 62)	17.31 (± 15.524)			
Week 26 (n= 216, 57, 211, 59, 60)	66.08 (± 16.098)			
Week 52 (n= 204, 60, 198, 60, 61)	65.89 (± 17.651)			
Week 78 (n= 0, 54, 0, 59, 58)	63.08 (± 21.364)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change from Baseline (%CfB) in serum Type I Collagen C-telopeptide (sCTX)

End point title	Percentage Change from Baseline (%CfB) in serum Type I Collagen C-telopeptide (sCTX)

End point description:

Percentage Change from Baseline in sCTX was assessed as part of pharmacodynamics parameter with US-licensed Prolia® was assessed in female subjects with postmenopausal osteoporosis.
PDS included all subjects in safety population with at least one evaluable PD parameter (%CfB and AUEC) and not had any protocol deviations that have a relevant impact on sCTX or serum P1NP results included in PD parameter calculation. Here, 'number of subjects analyzed' specifies all subjects who were evaluated for this outcome measure.
Here, 9999 indicates that the data were not available due to insufficient number of subjects.

End point type	Secondary

End point timeframe:

Weeks 4, 26, 52 and 78

End point values	RGB-14-P	RGB-14-P to RGB-14-P	Prolia®	Prolia® to RGB-14-P
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	234	60	220	60
Units: percent				
arithmetic mean (standard deviation)				
Week 4 (n= 234, 60, 220, 59, 62)	85.87 (± 9.567)	84.96 (± 11.206)	85.38 (± 15.501)	84.71 (± 23.071)
Week 26 (n= 216, 57, 211, 59, 60)	69.74 (± 23.212)	67.29 (± 23.572)	61.51 (± 83.764)	53.23 (± 147.679)
Week 52 (n= 204, 60, 198, 60, 61)	62.90 (± 28.995)	60.41 (± 31.958)	58.26 (± 63.927)	53.89 (± 94.853)
Week 78 (n= 0, 54, 0, 59, 59)	9999 (± 9999)	58.70 (± 34.117)	9999 (± 9999)	53.32 (± 42.855)

End point values	Prolia® to Prolia®			
Subject group type	Reporting group			
Number of subjects analysed	62			
Units: percent				
arithmetic mean (standard deviation)				
Week 4 (n= 234, 60, 220, 59, 62)	88.08 (± 5.832)			

Week 26 (n= 216, 57, 211, 59, 60)	71.27 (± 17.483)			
Week 52 (n= 204, 60, 198, 60, 61)	66.79 (± 24.151)			
Week 78 (n= 0, 54, 0, 59, 59)	57.38 (± 30.562)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Subjects with Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point description:

The safety and tolerability of RGB-14-P with US-licensed Prolia® in female subjects with postmenopausal osteoporosis was assessed.
Safety analysis set (SAF) included all subjects who received at least one full or partial dose of IMP.
Here, disc = discontinuation, IMP = Investigational Medicinal Product, s/ws = severe or worse severity

End point type	Secondary

End point timeframe:

Main Period: From screening (Weeks -5 to 0) to Week 52; Transition Period: From Week 52 to Week 78

End point values	RGB-14-P	RGB-14-P to RGB-14-P	Prolia®	Prolia® to RGB-14-P
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	242	63	231	62
Units: Subjects				
Any AE	161	0	158	0
Any TEAEs	158	30	152	25
Any TEAEs s/ws	8	0	9	1
Any treatment related TEAE	36	2	32	5
Any treatment related TEAE s/ws	1	0	0	0
Any serious TEAEs	7	0	16	0
Any serious TEAEs s/ws	5	0	9	0
Any non-serious TEAEs	158	30	149	25
Any AEs leading to subject disc	2	0	3	0
Any TEAEs leading to subject disc	2	0	3	0
Any treatment related TEAE leading to subject disc	1	0	0	0
Any TEAEs leading to disc of IMP	2	0	2	0
Any treatment related TEAE leading to disc of IMP	1	0	0	0
Any fracture TEAE	9	4	18	3
Any fracture TEAE s/ws	2	0	1	0
Any serious fracture TEAEs	1	0	1	0
Any serious fracture TEAEs s/ws	1	0	1	0
Deaths	0	0	1	0
Any AE leading to death	0	0	1	0

Any TEAE leading to death	0	0	1	0
Any injection site reactions	0	0	2	3
Any treatment related serious TEAE	0	0	0	0
Any treatment related serious TEAE s/ws	0	0	0	0
Any treatment related fracture TEAE	0	0	0	0
Any treatment related fracture TEAE s/ws	0	0	0	0
Any treatment related serious fracture TEAE	0	0	0	0
Any treatment related serious fracture TEAE s/ws	0	0	0	0
Any treatment related fatal serious TEAEs	0	0	0	0
Any injection site reactions of CTCAE grade ≥3	0	0	0	0
Any injection site reactions s/ws	0	0	0	0

End point values	Prolia® to Prolia®			
Subject group type	Reporting group			
Number of subjects analysed	63			
Units: Subjects				
Any AE	0			
Any TEAEs	25			
Any TEAEs s/ws	0			
Any treatment related TEAE	1			
Any treatment related TEAE s/ws	0			
Any serious TEAEs	0			
Any serious TEAEs s/ws	0			
Any non-serious TEAEs	25			
Any AEs leading to subject disc	0			
Any TEAEs leading to subject disc	0			
Any treatment related TEAE leading to subject disc	0			
Any TEAEs leading to disc of IMP	0			
Any treatment related TEAE leading to disc of IMP	0			
Any fracture TEAE	1			
Any fracture TEAE s/ws	0			
Any serious fracture TEAEs	0			
Any serious fracture TEAEs s/ws	0			
Deaths	0			
Any AE leading to death	0			
Any TEAE leading to death	0			
Any injection site reactions	1			
Any treatment related serious TEAE	0			
Any treatment related serious TEAE s/ws	0			
Any treatment related fracture TEAE	0			
Any treatment related fracture TEAE s/ws	0			

Any treatment related serious fracture TEAE	0			
Any treatment related serious fracture TEAE s/ws	0			
Any treatment related fatal serious TEAEs	0			
Any injection site reactions of CTCAE grade ≥3	0			
Any injection site reactions s/ws	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Anti-Drug Antibodies (ADAs)

End point title	Number of Subjects with Anti-Drug Antibodies (ADAs)

End point description:

Number of subjects with positive ADAs were assessed.
Immunogenicity analysis set (IAS) included all subjects in the safety population who had the pre-dose immunogenicity result and at least one available postbaseline immunogenicity assessment. Here, 'number of subjects analyzed' specifies all subjects who were evaluated for this outcome measure.
Here, 9999 indicates that data was not available due to insufficient number of subjects.

End point type	Secondary

End point timeframe:

Weeks 0, 2, 4, 26, 28, 30, 52, 54, 56 and 78

End point values	RGB-14-P	RGB-14-P to RGB-14-P	Prolia®	Prolia® to RGB-14-P
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	239	63	228	62
Units: Subjects				
Week 0 (n= 239, 63, 228, 62, 62)	0	0	1	0
Week 2 (n= 236, 63, 224, 60, 61)	2	0	0	0
Week 4 (n= 237, 63, 226, 60, 62)	0	0	0	0
Week 26 (n= 227, 63, 219, 62, 62)	0	0	0	0
Week 28 (n= 218, 60, 206, 58, 59)	0	0	1	0
Week 30 (n= 220, 63, 215, 62, 62)	0	0	1	0
Week 52 (n= 225, 63, 208, 62, 61)	0	0	0	0
Week 54 (n= 0, 62, 0, 61, 62)	9999	0	9999	0
Week 56 (n= 0, 63, 0, 62, 61)	9999	0	9999	0
Week 78 (n= 0, 63, 0, 62, 61)	9999	0	9999	0

End point values	Prolia® to Prolia®			
Subject group type	Reporting group			
Number of subjects analysed	62			
Units: Subjects				

Week 0 (n= 239, 63, 228, 62, 62)	0			
Week 2 (n= 236, 63, 224, 60, 61)	0			
Week 4 (n= 237, 63, 226, 60, 62)	0			
Week 26 (n= 227, 63, 219, 62, 62)	0			
Week 28 (n= 218, 60, 206, 58, 59)	1			
Week 30 (n= 220, 63, 215, 62, 62)	1			
Week 52 (n= 225, 63, 208, 62, 61)	0			
Week 54 (n= 0, 62, 0, 61, 62)	1			
Week 56 (n= 0, 63, 0, 62, 61)	1			
Week 78 (n= 0, 63, 0, 62, 61)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Neutralizing Antibodies

End point title	Number of Subjects with Neutralizing Antibodies

End point description:

Number of subjects with positive neutralizing antibodies were assessed.
IAS included all subjects in the safety population who had the pre-dose immunogenicity result and at least one available postbaseline immunogenicity assessment. Here, 'number of subjects analyzed' specifies all subjects who were evaluated for this outcome measure.
Here, 9999 indicates that the data were not available due to insufficient number of subjects.

End point type	Secondary

End point timeframe:

Weeks 0, 2, 4, 26, 28, 30, 52, 54, 56 and 78

End point values	RGB-14-P	RGB-14-P to RGB-14-P	Prolia®	Prolia® to RGB-14-P
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	0[8]	2	0[9]
Units: Subjects				
Week 0 (n= 0, 0, 1, 0, 0)	9999		9999	
Week 2 (n= 2, 0, 0, 0, 0)	1		9999	
Week 4 (n= 0, 0, 0, 0, 0)	9999		9999	
Week 26 (n= 0, 0, 0, 0, 0)	9999		9999	
Week 28 (n= 0, 0, 1, 0, 1)	9999		1	
Week 30 (n= 0, 0, 1, 0, 1)	9999		9999	
Week 52 (n= 0, 0, 0, 0, 0)	9999		9999	
Week 54 (n= 0, 0, 0, 0, 1)	9999		9999	
Week 56 (n= 0, 0, 0, 0, 1)	9999		9999	
Week 78 (n= 0, 0, 0, 0, 0)	9999		9999	

Notes:

[8] - Number of subjects analyzed were 0 due to no positive ADA response.

[9] - Number of subjects analyzed were 0 due to no positive ADA response.

End point values	Prolia® to Prolia®			

Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Subjects				
Week 0 (n= 0, 0, 1, 0, 0)	9999			
Week 2 (n= 2, 0, 0, 0, 0)	9999			
Week 4 (n= 0, 0, 0, 0, 0)	9999			
Week 26 (n= 0, 0, 0, 0, 0)	9999			
Week 28 (n= 0, 0, 1, 0, 1)	1			
Week 30 (n= 0, 0, 1, 0, 1)	9999			
Week 52 (n= 0, 0, 0, 0, 0)	9999			
Week 54 (n= 0, 0, 0, 0, 1)	1			
Week 56 (n= 0, 0, 0, 0, 1)	1			
Week 78 (n= 0, 0, 0, 0, 0)	9999			

Statistical analyses

No statistical analyses for this end point

Secondary: Titre of ADAs

End point title	Titre of ADAs

End point description:

The immunogenicity of RGB -14- P with US-licensed Prolia® in female subjects with postmenopausal osteoporosis was assessed.
IAS included all subjects in the safety population who had the pre-dose immunogenicity result and at least one available postbaseline immunogenicity assessment. Here, 'number of subjects analyzed' specifies all subjects who were evaluated for ADA.
The outcome measure in this table is the titer, N refers to all subjects analyzed for ADA. (Only 7 samples, from 4 subjects were evaluated for titer).
Here, '99999' indicates that titer was not evaluable due to no positive ADA response and '9999' indicates that data was not available due to insufficient number of subjects.

End point type	Secondary

End point timeframe:

Weeks 0, 2, 4, 26, 28, 30, 52, 54, 56 and 78

End point values	RGB-14-P	RGB-14-P to RGB-14-P	Prolia®	Prolia® to RGB-14-P
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	239	63	228	62
Units: titre				
median (full range (min-max))				
Week 0 (n= 239, 63, 228, 62, 62)	99999 (99999 to 99999)	99999 (99999 to 99999)	302.0 (302 to 302)	99999 (99999 to 99999)
Week 2 (n= 236, 63, 224, 60, 61)	761.0 (60 to 1462)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Week 4 (n= 237, 63, 226, 60, 62)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Week 26 (n= 227, 63, 219, 62, 62)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Week 28 (n= 218, 60, 206, 58, 59)	99999 (99999 to 99999)	99999 (99999 to 99999)	172.0 (172 to 172)	99999 (99999 to 99999)

Week 30 (n= 220, 63, 215, 62, 62)	99999 (99999 to 99999)	99999 (99999 to 99999)	211.0 (211 to 211)	99999 (99999 to 99999)
Week 52 (n= 225, 63, 208, 62, 61)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Week 54 (n= 0, 62, 0, 61, 62)	9999 (9999 to 9999)	99999 (99999 to 99999)	9999 (9999 to 9999)	99999 (99999 to 99999)
Week 56 (n= 0, 63, 0, 62, 61)	9999 (9999 to 9999)	99999 (99999 to 99999)	9999 (9999 to 9999)	99999 (99999 to 99999)
Week 78 (n= 0, 63, 0, 62, 61)	9999 (9999 to 9999)	99999 (99999 to 99999)	9999 (9999 to 9999)	99999 (99999 to 99999)

End point values	Prolia® to Prolia®			
Subject group type	Reporting group			
Number of subjects analysed	62			
Units: titre				
median (full range (min-max))				
Week 0 (n= 239, 63, 228, 62, 62)	99999 (99999 to 99999)			
Week 2 (n= 236, 63, 224, 60, 61)	99999 (99999 to 99999)			
Week 4 (n= 237, 63, 226, 60, 62)	99999 (99999 to 99999)			
Week 26 (n= 227, 63, 219, 62, 62)	99999 (99999 to 99999)			
Week 28 (n= 218, 60, 206, 58, 59)	172.0 (172 to 172)			
Week 30 (n= 220, 63, 215, 62, 62)	211.0 (211 to 211)			
Week 52 (n= 225, 63, 208, 62, 61)	99999 (99999 to 99999)			
Week 54 (n= 0, 62, 0, 61, 62)	224.0 (224 to 224)			
Week 56 (n= 0, 63, 0, 62, 61)	152.0 (152 to 152)			
Week 78 (n= 0, 63, 0, 62, 61)	99999 (99999 to 99999)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Main Period: From screening (Weeks -5 to 0) to Week 52; Transition Period: From Week 52 to Week 78	
Adverse event reporting additional description:	
Safety analysis set included all subjects who received at least one full or partial dose of IMP.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups	
Reporting group title	RGB-14-P
Reporting group description:	
Subjects received RGB-14-P as subcutaneous (SC) injection on Day 1 of treatment period 1 (week 0) and treatment period 2 (week 26).	
Reporting group title	Prolia®
Reporting group description:	
Subjects received Prolia® as SC injection on Day 1 of treatment period 1 (week 0) and treatment period 2 (week 26).	
Reporting group title	RGB-14-P to RGB-14-P
Reporting group description:	
Subjects who received RGB-14-P during the main period were re-randomized and received Prolia® as SC injection on day 1 of treatment period 3 (week 52).	
Reporting group title	Prolia® to RGB-14-P
Reporting group description:	
Subjects who received Prolia® during the main period were re-randomized and received RGB-14-P as SC injection on Day 1 of treatment period 3 (week 52).	
Reporting group title	Prolia® to Prolia®
Reporting group description:	
Subjects who received Prolia® during the main period were re-randomized and received Prolia® as SC injection on Day 1 of treatment period 3 (week 52).	

Serious adverse events	RGB-14-P	Prolia®	RGB-14-P to RGB-14-P
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 242 (2.89%)	16 / 231 (6.93%)	0 / 63 (0.00%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events			0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	0 / 242 (0.00%)	1 / 231 (0.43%)	0 / 63 (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
Breast cancer			

subjects affected / exposed	0 / 242 (0.00%)	1 / 231 (0.43%)	0 / 63 (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
Clear cell renal cell carcinoma			
subjects affected / exposed	0 / 242 (0.00%)	1 / 231 (0.43%)	0 / 63 (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
Follicular lymphoma			
subjects affected / exposed	0 / 242 (0.00%)	1 / 231 (0.43%)	0 / 63 (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
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 242 (0.00%)	1 / 231 (0.43%)	0 / 63 (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
Renal neoplasm			
subjects affected / exposed	0 / 242 (0.00%)	1 / 231 (0.43%)	0 / 63 (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
Thyroid cancer			
subjects affected / exposed	1 / 242 (0.41%)	0 / 231 (0.00%)	0 / 63 (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
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	1 / 242 (0.41%)	0 / 231 (0.00%)	0 / 63 (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
Meniscus injury			
subjects affected / exposed	1 / 242 (0.41%)	1 / 231 (0.43%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			

subjects affected / exposed	0 / 242 (0.00%)	1 / 231 (0.43%)	0 / 63 (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
Tendon rupture			
subjects affected / exposed	0 / 242 (0.00%)	1 / 231 (0.43%)	0 / 63 (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
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 242 (0.00%)	1 / 231 (0.43%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 242 (0.00%)	1 / 231 (0.43%)	0 / 63 (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 / 242 (0.00%)	1 / 231 (0.43%)	0 / 63 (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
Cardiac disorder			
subjects affected / exposed	0 / 242 (0.00%)	1 / 231 (0.43%)	0 / 63 (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
Cardiac failure chronic			
subjects affected / exposed	0 / 242 (0.00%)	1 / 231 (0.43%)	0 / 63 (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
Coronary artery stenosis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 231 (0.43%)	0 / 63 (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 / 242 (0.00%)	1 / 231 (0.43%)	0 / 63 (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
Nervous system disorders			
Lumbosacral radiculopathy			
subjects affected / exposed	1 / 242 (0.41%)	0 / 231 (0.00%)	0 / 63 (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
Gastrointestinal disorders			
Chronic gastritis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 231 (0.43%)	0 / 63 (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
Reproductive system and breast disorders			
Endometrial disorder			
subjects affected / exposed	0 / 242 (0.00%)	1 / 231 (0.43%)	0 / 63 (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			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 242 (0.41%)	1 / 231 (0.43%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety disorder			
subjects affected / exposed	1 / 242 (0.41%)	0 / 231 (0.00%)	0 / 63 (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
Panic attack			
subjects affected / exposed	1 / 242 (0.41%)	0 / 231 (0.00%)	0 / 63 (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			

Muscular weakness			
subjects affected / exposed	0 / 242 (0.00%)	1 / 231 (0.43%)	0 / 63 (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
Osteoarthritis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 231 (0.00%)	0 / 63 (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
Rotator cuff syndrome			
subjects affected / exposed	0 / 242 (0.00%)	1 / 231 (0.43%)	0 / 63 (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			
Pneumonia			
subjects affected / exposed	1 / 242 (0.41%)	0 / 231 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Prolia® to RGB-14-P	Prolia® to Prolia®	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	
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)			
Bladder cancer			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (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 / 62 (0.00%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Follicular lymphoma			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal neoplasm			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid cancer			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (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			
Humerus fracture			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			

subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (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 coronary syndrome			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (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 / 62 (0.00%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorder			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure chronic			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (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 / 62 (0.00%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			

Lumbosacral radiculopathy			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Chronic gastritis			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (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 disorder			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (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			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety disorder			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Panic attack			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (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			
Muscular weakness			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (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 / 62 (0.00%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (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			
Pneumonia			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	RGB-14-P	Prolia®	RGB-14-P to RGB-14-P
Total subjects affected by non-serious adverse events			
subjects affected / exposed	100 / 242 (41.32%)	85 / 231 (36.80%)	4 / 63 (6.35%)
Vascular disorders			
Hypertension			
subjects affected / exposed	8 / 242 (3.31%)	13 / 231 (5.63%)	0 / 63 (0.00%)
occurrences (all)	9	14	0
Nervous system disorders			
Headache			
subjects affected / exposed	14 / 242 (5.79%)	4 / 231 (1.73%)	0 / 63 (0.00%)
occurrences (all)	15	5	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	12 / 242 (4.96%)	10 / 231 (4.33%)	0 / 63 (0.00%)
occurrences (all)	16	13	0
Infections and infestations			
COVID-19			
subjects affected / exposed	25 / 242 (10.33%)	24 / 231 (10.39%)	0 / 63 (0.00%)
occurrences (all)	25	25	0
Nasopharyngitis			

subjects affected / exposed	23 / 242 (9.50%)	21 / 231 (9.09%)	1 / 63 (1.59%)
occurrences (all)	29	28	1
Upper respiratory tract infection			
subjects affected / exposed	23 / 242 (9.50%)	11 / 231 (4.76%)	0 / 63 (0.00%)
occurrences (all)	34	13	0
Urinary tract infection			
subjects affected / exposed	11 / 242 (4.55%)	11 / 231 (4.76%)	0 / 63 (0.00%)
occurrences (all)	13	17	0
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	22 / 242 (9.09%)	22 / 231 (9.52%)	3 / 63 (4.76%)
occurrences (all)	31	27	3

Non-serious adverse events	Prolia® to RGB-14-P	Prolia® to Prolia®	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 62 (4.84%)	6 / 63 (9.52%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	
occurrences (all)	0	0	
Nasopharyngitis			
subjects affected / exposed	2 / 62 (3.23%)	4 / 63 (6.35%)	
occurrences (all)	2	4	
Upper respiratory tract infection			

subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	
occurrences (all)	0	0	
Urinary tract infection			
subjects affected / exposed	0 / 62 (0.00%)	0 / 63 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	1 / 62 (1.61%)	2 / 63 (3.17%)	
occurrences (all)	1	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 August 2021	The protocol was amended to Substantial Amendment 1, dated 03 Aug 2021, to incorporate and implement responses and suggestions made by the USFDA.
10 January 2022	The protocol was amended to Substantial Amendment 2, dated 10 Jan 2022, to incorporate and implement changes for statistical analysis, consistency with supporting study documents and suggestions made based on Investigator experiences.
19 January 2023	The protocol was amended to Substantial Amendment 3, dated 19 Jan 2023, to incorporate and implement 10% increase in the number of subjects to be enrolled for the Transition Period to meet the requirements of USFDA, considering the drop-out was higher than expected.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported