Clinical trial results:
A Randomized, Non-Inferiority, Phase 3, Open-Label, Multicenter Study to Evaluate the Efficacy and Safety of Abaloparatide-sMTS for the Treatment of Postmenopausal Women with Osteoporosis (the wearABLe Study)

Summary

EudraCT number	2019-004807-11
Trial protocol	HU DK BG
Global end of trial date	09 November 2021

Results information

Result version number	v2 (current)
This version publication date	31 March 2023
First version publication date	25 December 2022
Version creation reason	• Correction of full data set Revisions to align with ClinicalTrials.gov posting.

Trial information

Trial identification

Sponsor protocol code	BA058-05-021

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04064411
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Radius Health, Inc.
Sponsor organisation address	22 Boston Wharf Road, 7th floor, Boston, MA, United States, 02210
Public contact	Radius Contact Information, Radius Health Inc., 1 6175514000, info@radiuspharm.com
Scientific contact	Radius Contact Information, Radius Health, Inc., 1 6175514000, info@radiuspharm.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	09 November 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 October 2021
Global end of trial reached?	Yes
Global end of trial date	09 November 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

A 12-month study to compare the efficacy and safety of abaloparatide-solid microstructured transdermal system (sMTS) with abaloparatide-subcutaneous (SC).

Protection of trial subjects:

The study was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki, the guidelines for current Good Clinical Practice International Conference on Harmonization (ICH), the US Food and Drug Administration Code of Federal Regulations, and all other applicable local regulatory and ethical requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 August 2019
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: 352
Country: Number of subjects enrolled	Denmark: 16
Country: Number of subjects enrolled	Hungary: 29
Country: Number of subjects enrolled	Poland: 114
Worldwide total number of subjects	511
EEA total number of subjects	159

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)	111

From 65 to 84 years	400
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Eligible female participants were randomized to a 12-month open-label study treatment at 83 study centers in the United States, Denmark, Hungary, and Poland.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor[1]

Blinding implementation details:

Treatment was not blinded to either the participants or investigators because of the differences in how study drug was administered. However, the central imaging laboratory responsible for measuring BMD was blinded to the participant's treatment assignment throughout the study.

Arms

Are arms mutually exclusive?	Yes
Arm title	Abaloparatide-SC

Arm description:

Participants self-administered daily doses of abaloparatide 80 micrograms (mcg) SC for 12 months using a single-participant, multiple-use, prefilled injection pen that delivers 30 doses. Participants received a new injection pen every 30 days.

Arm type	Experimental
Investigational medicinal product name	abaloparatide
Investigational medicinal product code	
Other name	TYMLOS®, BA058, abaloparatide-SC
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Abaloparatide was administered per dose and schedule specified in the arm description.

Arm title	Abaloparatide-sMTS

Arm description:

Participants self-administered abaloparatide-sMTS 300 mcg applied to the thigh for 5 minutes daily for 12 months.

Arm type	Active comparator
Investigational medicinal product name	abaloparatide solid microstructured transdermal system
Investigational medicinal product code	
Other name	BA058, abaloparatide-transdermal
Pharmaceutical forms	Transdermal system
Routes of administration	Transdermal use

Dosage and administration details:

Abaloparatide-sMTS was administered per dose and schedule specified in the arm description.

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Treatment was not blinded to either the participants or Investigators because of the differences in how study drug was administered.

Number of subjects in period 1	Abaloparatide-SC	Abaloparatide-sMTS
Started	255	256
Received at Least 1 Dose of Study Drug	254	252
Completed	191	201
Not completed	64	55
Adverse event, serious fatal	1	-
Consent withdrawn by subject	25	29
Adverse event, non-fatal	29	19
Protocol Deviation	-	2
Significant Deterioration from Baseline of BMD	-	2
Other than Specified	4	1
Lost to follow-up	5	2

Baseline characteristics

Reporting groups	
Reporting group title	Abaloparatide-SC
Reporting group description:	
Participants self-administered daily doses of abaloparatide 80 micrograms (mcg) SC for 12 months using a single-participant, multiple-use, prefilled injection pen that delivers 30 doses. Participants received a new injection pen every 30 days.	
Reporting group title	Abaloparatide-sMTS
Reporting group description:	
Participants self-administered abaloparatide-sMTS 300 mcg applied to the thigh for 5 minutes daily for 12 months.	

Reporting group values	Abaloparatide-SC	Abaloparatide-sMTS	Total
Number of subjects	255	256	511
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)	59	52	111
From 65-84 years	196	204	400
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	68.8	69.3	
standard deviation	± 6.87	± 6.49	-
Sex: Female, Male Units: participants			
Female	255	256	511
Male	0	0	0
Race Units: Subjects			
White	248	243	491
Black or African American	4	4	8
Asian	1	1	2
American Indian or Alaska Native	0	1	1
Multiple	0	3	3
Other	2	4	6
Ethnicity Units: Subjects			
Hispanic or Latino	27	24	51
Not Hispanic or Latino	227	230	457
Unknown	1	2	3

Lumbar Spine BMD T-Score			
The BMD T-score is the BMD, assessed by dual energy x-ray absorptiometry (DXA), at the site when compared to that of a healthy woman (20 to 29 years old). Normal is a T-score of -1.0 or higher; Osteopenia is defined as between -1.0 and -2.5; Osteoporosis is defined as -2.5 or lower, meaning a bone density that is two and a half standard deviations below the mean of a woman (20 to 29 years old). Lower T-scores indicate worse bone condition. Analysis includes participants who had lumbar spine BMD T-Score assessment at baseline.			
Units: T-Score			
arithmetic mean	-2.569	-2.554	
standard deviation	± 1.1534	± 1.0997	-

End points

End points reporting groups

Reporting group title	Abaloparatide-SC
Reporting group description:	
Participants self-administered daily doses of abaloparatide 80 micrograms (mcg) SC for 12 months using a single-participant, multiple-use, prefilled injection pen that delivers 30 doses. Participants received a new injection pen every 30 days.	
Reporting group title	Abaloparatide-sMTS
Reporting group description:	
Participants self-administered abaloparatide-sMTS 300 mcg applied to the thigh for 5 minutes daily for 12 months.	

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:	
Lumbar Spine BMD was assessed by DXA scans evaluated by a central imaging laboratory.	
End point type	Primary
End point timeframe:	
Baseline, Month 12	

End point values	Abaloparatide-SC	Abaloparatide-sMTS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	200		
Units: percent change				
least squares mean (standard error)	10.8571 (± 0.4755)	7.1361 (± 0.4605)		

Statistical analyses

Statistical analysis title	Percent Change from Baseline in Lumbar Spine BMD
Statistical analysis description:	
Percent change from baseline in lumbar spine BMD at Month 12.	
Comparison groups	Abaloparatide-SC v Abaloparatide-sMTS
Number of subjects included in analysis	389
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Least Squares Means (LSM) Difference
Point estimate	-3.721

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.0089
upper limit	-2.4331

Notes:

[1] - Noninferiority margin = 2.0% for abaloparatide-sMTS compared with abaloparatide-SC. Non-inferiority was to be concluded if the lower bound of the 2-sided 95% Confidence Interval (CI) for the estimated treatment difference (abaloparatide-sMTS minus abaloparatide-SC) in the percent change from baseline in lumbar spine BMD at 12 months was above -2.0% using a Mixed Model for Repeated Measures (MMRM) analysis.

Secondary: Percent Change from Baseline in Total Hip BMD at Month 12

End point title	Percent Change from Baseline in Total Hip BMD at Month 12

End point description:

Total hip BMD was assessed by DXA scans evaluated by a central imaging laboratory.

End point type	Secondary

End point timeframe:

Baseline, Month 12

End point values	Abaloparatide-SC	Abaloparatide-sMTS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	188	200		
Units: percent change				
least squares mean (standard error)	3.6995 (± 0.2776)	1.9688 (± 0.2675)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in Femoral Neck BMD at Month 12

End point title	Percent Change from Baseline in Femoral Neck BMD at Month 12

End point description:

Femoral neck BMD was assessed by DXA scans evaluated by a central imaging laboratory.

End point type	Secondary

End point timeframe:

Baseline, Month 12

End point values	Abaloparatide-SC	Abaloparatide-sMTS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	188	200		
Units: percent change				
least squares mean (standard error)	3.4159 (± 0.3750)	1.9163 (± 0.3599)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline through Month 13	
Adverse event reporting additional description:	
All-Cause Mortality, Serious, and Other Adverse Events were assessed in the Safety Population: All randomized participants who received at least 1 dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	Abaloparatide-SC
Reporting group description:	
Participants self-administered daily doses of abaloparatide 80 mcg SC for 12 months using a single-participant, multiple-use, prefilled injection pen that delivers 30 doses. Participants received a new injection pen every 30 days.	
Reporting group title	Abaloparatide-sMTS
Reporting group description:	
Participants self-administered abaloparatide-sMTS 300 mcg applied to the thigh for 5 minutes daily for 12 months.	

Serious adverse events	Abaloparatide-SC	Abaloparatide-sMTS	
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 254 (7.48%)	16 / 252 (6.35%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	1	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Intraductal proliferative breast lesion			
subjects affected / exposed	1 / 254 (0.39%)	0 / 252 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma stage IV			
subjects affected / exposed	1 / 254 (0.39%)	0 / 252 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Invasive ductal breast carcinoma			

subjects affected / exposed	1 / 254 (0.39%)	0 / 252 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	1 / 254 (0.39%)	0 / 252 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 254 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	1 / 254 (0.39%)	0 / 252 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 254 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	2 / 254 (0.79%)	0 / 252 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 254 (0.39%)	0 / 252 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			

subjects affected / exposed	0 / 254 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	1 / 254 (0.39%)	0 / 252 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	1 / 254 (0.39%)	0 / 252 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	0 / 254 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	0 / 254 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	1 / 254 (0.39%)	0 / 252 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	1 / 254 (0.39%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	0 / 254 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			

subjects affected / exposed	1 / 254 (0.39%)	0 / 252 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bundle branch block left			
subjects affected / exposed	0 / 254 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 254 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 254 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Metabolic encephalopathy			
subjects affected / exposed	1 / 254 (0.39%)	0 / 252 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Normal pressure hydrocephalus			
subjects affected / exposed	0 / 254 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient global amnesia			
subjects affected / exposed	0 / 254 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain oedema			
subjects affected / exposed	0 / 254 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			

subjects affected / exposed	0 / 254 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Iridocyclitis			
subjects affected / exposed	1 / 254 (0.39%)	0 / 252 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 254 (0.39%)	0 / 252 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cannabinoid hyperemesis syndrome			
subjects affected / exposed	0 / 254 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	0 / 254 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 254 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 254 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Polyarthritis			

subjects affected / exposed	0 / 254 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	1 / 254 (0.39%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 254 (0.39%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	2 / 254 (0.79%)	0 / 252 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 254 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	1 / 254 (0.39%)	0 / 252 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	0 / 254 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 254 (0.39%)	0 / 252 (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: 5 %

Non-serious adverse events	Abaloparatide-SC	Abaloparatide-sMTS	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	204 / 254 (80.31%)	239 / 252 (94.84%)	
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	20 / 254 (7.87%)	19 / 252 (7.54%)	
occurrences (all)	27	20	
Hypertension			
subjects affected / exposed	15 / 254 (5.91%)	8 / 252 (3.17%)	
occurrences (all)	16	8	
Cardiac disorders			
Palpitations			
subjects affected / exposed	18 / 254 (7.09%)	6 / 252 (2.38%)	
occurrences (all)	22	7	
Nervous system disorders			
Headache			
subjects affected / exposed	41 / 254 (16.14%)	25 / 252 (9.92%)	
occurrences (all)	46	28	
Dizziness			
subjects affected / exposed	24 / 254 (9.45%)	17 / 252 (6.75%)	
occurrences (all)	28	18	
General disorders and administration site conditions			
Administration site erythema			
subjects affected / exposed	4 / 254 (1.57%)	13 / 252 (5.16%)	
occurrences (all)	4	13	
Application site swelling			
subjects affected / exposed	6 / 254 (2.36%)	116 / 252 (46.03%)	
occurrences (all)	6	124	
Application site oedema			
subjects affected / exposed	1 / 254 (0.39%)	122 / 252 (48.41%)	
occurrences (all)	1	128	
Application site discolouration			
subjects affected / exposed	0 / 254 (0.00%)	37 / 252 (14.68%)	
occurrences (all)	0	37	

Application site haemorrhage			
subjects affected / exposed	2 / 254 (0.79%)	73 / 252 (28.97%)	
occurrences (all)	2	78	
Application site erythema			
subjects affected / exposed	15 / 254 (5.91%)	190 / 252 (75.40%)	
occurrences (all)	15	205	
Application site vesicles			
subjects affected / exposed	1 / 254 (0.39%)	16 / 252 (6.35%)	
occurrences (all)	1	16	
Application site reaction			
subjects affected / exposed	0 / 254 (0.00%)	18 / 252 (7.14%)	
occurrences (all)	0	20	
Application site pruritus			
subjects affected / exposed	10 / 254 (3.94%)	83 / 252 (32.94%)	
occurrences (all)	10	87	
Application site pain			
subjects affected / exposed	14 / 254 (5.51%)	142 / 252 (56.35%)	
occurrences (all)	23	289	
Injection site pain			
subjects affected / exposed	82 / 254 (32.28%)	17 / 252 (6.75%)	
occurrences (all)	164	26	
Injection site erythema			
subjects affected / exposed	119 / 254 (46.85%)	26 / 252 (10.32%)	
occurrences (all)	131	27	
Injection site haemorrhage			
subjects affected / exposed	30 / 254 (11.81%)	6 / 252 (2.38%)	
occurrences (all)	30	6	
Injection site swelling			
subjects affected / exposed	48 / 254 (18.90%)	10 / 252 (3.97%)	
occurrences (all)	49	10	
Fatigue			
subjects affected / exposed	14 / 254 (5.51%)	6 / 252 (2.38%)	
occurrences (all)	14	7	
Injection site bruising			
subjects affected / exposed	35 / 254 (13.78%)	1 / 252 (0.40%)	
occurrences (all)	37	1	

Injection site oedema			
subjects affected / exposed	31 / 254 (12.20%)	12 / 252 (4.76%)	
occurrences (all)	32	12	
Injection site pruritus			
subjects affected / exposed	48 / 254 (18.90%)	9 / 252 (3.57%)	
occurrences (all)	51	9	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	35 / 254 (13.78%)	14 / 252 (5.56%)	
occurrences (all)	49	14	
Renal and urinary disorders			
Hypercalciuria			
subjects affected / exposed	6 / 254 (2.36%)	13 / 252 (5.16%)	
occurrences (all)	7	13	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	26 / 254 (10.24%)	14 / 252 (5.56%)	
occurrences (all)	34	14	
Arthralgia			
subjects affected / exposed	20 / 254 (7.87%)	25 / 252 (9.92%)	
occurrences (all)	25	29	
Pain in extremity			
subjects affected / exposed	17 / 254 (6.69%)	11 / 252 (4.37%)	
occurrences (all)	19	15	
Infections and infestations			
COVID-19			
subjects affected / exposed	18 / 254 (7.09%)	9 / 252 (3.57%)	
occurrences (all)	18	10	
Urinary tract infection			
subjects affected / exposed	20 / 254 (7.87%)	23 / 252 (9.13%)	
occurrences (all)	20	27	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 June 2019	• Updated inclusion criterion 3 for previous fractures to clarify that participants were required to meet only 1 and not both of the fracture requirements • Added that if sensitization was suspected, the Investigator was to contact the Sponsor for further instructions • Removed the requirement for the signing of an additional Informed Consent Form advising participants who sustained an incident fracture and elected to remain in the study that they were at increased risk for a subsequent fracture • Added that the radiographs of the lateral thoracic and lumbar spine at Screening would be assessed locally using the Genant Semi-Quantitative Scoring Method
17 June 2019	• Updated inclusion criterion for postmenopausal women as either a history of amenorrhea for at least 5 years or by an elevated follicle-stimulating hormone (FSH) value ≥30 International units per litre (IU/L) • Added that any subject with a thyroid stimulating hormone (TSH) value outside of the normal range was required to have T3 and free T4 tested, with results within the normal range in order to be enrolled • Added that bone-specific alkaline phosphatase testing was required only if alkaline phosphatase levels were outside of the normal range • Reduced the frequency of 4 hour postdose blood draws for evaluation of calcium
01 October 2019	• Removed the FSH value ≥30 IU/L from inclusion criterion for postmenopausal women

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: