Clinical trial results:
A Randomized, Double-blind, Placebo-controlled, Phase 3 Multicenter Study to Evaluate the Safety and Efficacy of Abaloparatide-SC for the Treatment of Men with Osteoporosis

Summary

EudraCT number	2017-004220-30
Trial protocol	PL IT
Global end of trial date	08 September 2021

Results information

Result version number	v1 (current)
This version publication date	24 May 2023
First version publication date	24 May 2023

Trial information

Trial identification

Sponsor protocol code	BA058-05-019

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03512262
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	14 February 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 August 2021
Global end of trial reached?	Yes
Global end of trial date	08 September 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this prospective controlled study is to evaluate the efficacy and the safety of abaloparatide 80 micrograms (mcg) per day administered subcutaneously (SC) compared to placebo in men with osteoporosis. Efficacy was primarily assessed by the change in bone mineral density (BMD) over 12 months.

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	03 May 2018
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: 108
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Canada: 18
Country: Number of subjects enrolled	United States: 101
Worldwide total number of subjects	228
EEA total number of subjects	109

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)	59
From 65 to 84 years	168
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants who remained eligible for study participation were randomly allocated, using a 2:1 randomization ratio (abaloparatide:placebo) on Day 1, to receive treatment with either blinded abaloparatide 80 micrograms (mcg) per day or daily placebo subcutaneous (SC) injections.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Blinding implementation details:

Treatment was blinded to participants, investigators, outcome assessor and care provider throughout the study except in a medical emergency where the identity of study medication is necessary for participant treatment.

Arms

Are arms mutually exclusive?	Yes
Arm title	Abaloparatide

Arm description:

Participants self-administered daily doses of abaloparatide 80 mcg SC 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	BA058
Other name	TYMLOS®, 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	Placebo

Arm description:

Participants self-administered daily doses of placebo SC using a single-participant, multiple-use, prefilled injection pen that delivers 30 doses. Participants received a new injection pen every 30 days.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

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

Number of subjects in period 1	Abaloparatide	Placebo
Started	149	79
Received at Least 1 Dose of Study Drug	149	79
Completed	114	64
Not completed	35	15
Consent withdrawn by subject	17	9
Adverse event, non-fatal	8	3
Other than Specified	2	2
Lost to follow-up	7	1
Death (non-treatment emergent)	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Abaloparatide
Reporting group description:	
Participants self-administered daily doses of abaloparatide 80 mcg SC 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	Placebo
Reporting group description:	
Participants self-administered daily doses of placebo SC using a single-participant, multiple-use, prefilled injection pen that delivers 30 doses. Participants received a new injection pen every 30 days.	

Reporting group values	Abaloparatide	Placebo	Total
Number of subjects	149	79	228
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)	38	21	59
From 65-84 years	110	58	168
85 years and over	1	0	1
Age Continuous			
Units: years			
arithmetic mean	68.5	67.8	
standard deviation	± 8.25	± 8.53	-
Sex: Female, Male			
Units: participants			
Female	0	0	0
Male	149	79	228
Lumbar Spine Bone Mineral Density (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 thirty-year-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 man/woman (20 to 29 years old). Lower T-scores indicate worse bone condition.			
Units: BMD T-Score			
arithmetic mean	-2.11	-2.05	
standard deviation	± 1.119	± 1.217	-

End points

End points reporting groups

Reporting group title	Abaloparatide
Reporting group description:	
Participants self-administered daily doses of abaloparatide 80 mcg SC 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	Placebo
Reporting group description:	
Participants self-administered daily doses of placebo SC using a single-participant, multiple-use, prefilled injection pen that delivers 30 doses. Participants received a new injection pen every 30 days.	

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. Lumbar spine scans included L1 through L4. Positive changes from baseline indicate improvement in bone health	
End point type	Primary
End point timeframe:	
Baseline, Month 12	

End point values	Abaloparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	66		
Units: percent change				
least squares mean (standard error)	8.4820 (± 0.5353)	1.1654 (± 0.7235)		

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 v Placebo
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [1]
Method	ANCOVA
Parameter estimate	Least Squares (LSM) Means Difference
Point estimate	7.3165

Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	5.0668
upper limit	9.5663

Notes:

[1] - Significance level of 0.01.

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.
Positive changes from baseline indicate improvement in bone health.

End point type	Secondary

End point timeframe:

Baseline, Month 12

End point values	Abaloparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	66		
Units: percent change				
least squares mean (standard error)	2.1351 (± 0.2711)	0.0143 (± 0.3543)		

Statistical analyses

Statistical analysis title	Percent Change from Baseline in Total Hip BMD

Statistical analysis description:

Percent change from baseline in total hip BMD at Month 12.

Comparison groups	Abaloparatide v Placebo
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [2]
Method	ANCOVA
Parameter estimate	LSM Difference
Point estimate	2.1209
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	0.9948
upper limit	3.2469

Notes:

[2] - Significance level of 0.01.

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.
Positive changes from baseline indicate improvement in bone health

End point type	Secondary

End point timeframe:

Baseline, Month 12

End point values	Abaloparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	66		
Units: percent change				
least squares mean (standard error)	2.9766 (± 0.3448)	0.1545 (± 0.4527)		

Statistical analyses

Statistical analysis title	Percent Change from Baseline in Femoral Neck BMD

Statistical analysis description:

Percent change from baseline in femoral neck BMD at Month 12.

Comparison groups	Abaloparatide v Placebo
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [3]
Method	ANCOVA
Parameter estimate	LSM Difference
Point estimate	2.8221
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	1.3972
upper limit	4.2471

Notes:

[3] - Significance level of 0.01.

Secondary: Percent Change from Baseline in Lumbar Spine BMD at Month 6

End point title	Percent Change from Baseline in Lumbar Spine BMD at Month 6

End point description:

Lumbar Spine BMD was assessed by DXA scans evaluated by a central imaging laboratory. Lumbar spine scans included L1 through L4.
Positive changes from baseline indicate improvement in bone health.

End point type	Secondary

End point timeframe:

Baseline, Month 6

End point values	Abaloparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	123	70		
Units: percent change				
least squares mean (standard error)	5.5436 (± 0.4127)	0.6418 (± 0.5472)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Total Hip BMD From Baseline at Month 6

End point title	Percent Change in Total Hip BMD From Baseline at Month 6

End point description:

Total hip BMD was assessed by DXA scans evaluated by a central imaging laboratory.
Positive changes from baseline indicate improvement in bone health.

End point type	Secondary

End point timeframe:

Baseline, Month 6

End point values	Abaloparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	122	70		
Units: percent change				
least squares mean (standard error)	1.3888 (± 0.2142)	0.0267 (± 0.2790)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in Femoral Neck BMD at Month 6

End point title	Percent Change from Baseline in Femoral Neck BMD at Month 6

End point description:

Femoral neck BMD was assessed by DXA scans evaluated by a central imaging laboratory.
Positive changes from baseline indicate improvement in bone health.

End point type	Secondary

End point timeframe:

Baseline, Month 6

End point values	Abaloparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	122	70		
Units: percent change				
least squares mean (standard error)	1.4790 (± 0.2714)	-0.1884 (± 0.3569)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in Ultra-Distal Radius BMD at Month 12

End point title	Percent Change from Baseline in Ultra-Distal Radius BMD at Month 12

End point description:

Ultra-distal radius BMD was assessed by DXA scans.
Positive changes from baseline indicate improvement in bone health.

End point type	Secondary

End point timeframe:

Baseline, Month 12

End point values	Abaloparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	61		
Units: percent change				
least squares mean (standard error)	1.4358 (± 0.4236)	-0.1915 (± 0.5722)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in Distal One-third Radius BMD at Month 12

End point title	Percent Change from Baseline in Distal One-third Radius BMD at Month 12

End point description:

Distal one-third radius BMD was assessed by DXA scans.
Positive changes from baseline indicate improvement in bone health.

End point type	Secondary

End point timeframe:

Baseline, Month 12

End point values	Abaloparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	61		
Units: percent change				
least squares mean (standard error)	-0.0138 (± 0.3253)	0.7066 (± 0.4285)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Serum Procollagen Type I N-terminal Propeptide (s-PINP) at Month 12

End point title	Percent Change From Baseline in Serum Procollagen Type I N-terminal Propeptide (s-PINP) at Month 12

End point description:

Blood samples were taken to measure s-PINP, a bone formation marker. s-PINP concentrations reflect the rate of skeletal new bone formation. Increases in s-PINP indicate anabolic biologic response in the bone.

End point type	Secondary

End point timeframe:

Baseline, Month 12

End point values	Abaloparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	65		
Units: percent change				
arithmetic mean (standard deviation)	225.919 (± 416.4173)	0.291 (± 31.8038)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Serum Carboxy-terminal Cross-linking Telopeptide of Type I Collagen (s-CTX) at Month 12

End point title	Percent Change From Baseline in Serum Carboxy-terminal Cross-linking Telopeptide of Type I Collagen (s-CTX) at Month 12

End point description:

Blood samples were taken to measure s-CTX. Elevated levels of s-CTX indicate increased bone resorption (bone loss).

End point type	Secondary

End point timeframe:

Baseline, Month 12

End point values	Abaloparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	65		
Units: percent change				
arithmetic mean (standard deviation)	89.639 (± 206.7227)	15.359 (± 40.3351)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With New Clinical Fractures

End point title	Number of Participants With New Clinical Fractures

End point description:

Radiological evaluations were performed to identify any new clinical fractures (occurring after the screening visit).

End point type	Secondary

End point timeframe:

Baseline through Month 12

End point values	Abaloparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	79		
Units: participants				
number (not applicable)	1	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Participants with Change in Disease Status

End point title	Percent of Participants with Change in Disease Status

End point description:

The percentage of participants converting from the categories of osteoporosis to osteopenia or from

osteopenia to normal at End of Treatment (Month 12) was assessed.
Osteoporosis was defined as lumbar spine or total hip BMD T-score ≤ -2.5.
Osteopenia was defined as one of the following: 1) Lumbar spine > -2.5 and total hip BMD T-score > -2.5 and < -1.0; 2) Lumbar spine > -2.5 and < -1.0 and total hip BMD T-score > -2.5.
Normal was defined as lumbar spine and total hip BMD T-score ≥ -1.0.

End point type	Secondary

End point timeframe:

Baseline through Month 12

End point values	Abaloparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	142	75		
Units: percentage of participants				
number (not applicable)				
Osteopenia to Normal	8.8	8.0		
Osteopenia to Osteoporosis	0	12.0		
Osteoporosis to Normal	2.9	0		
Osteoporosis to Osteopenia	57.1	12.8		
Normal to Osteopenia or Osteoporosis	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Participants Experiencing BMD Gains from Baseline of > 0%, > 3%, and > 6% at the Lumbar Spine, Femoral Neck, and Total Hip

End point title	Percent of Participants Experiencing BMD Gains from Baseline of > 0%, > 3%, and > 6% at the Lumbar Spine, Femoral Neck, and Total Hip

End point description:

Lumbar spine, femoral neck, and total hip BMD were assessed by DXA scans evaluated by a central imaging laboratory.

End point type	Secondary

End point timeframe:

Month 12

End point values	Abaloparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	66		
Units: percentage of participants				
number (not applicable)				
BMD Increase >0% at All Three Sites	67.2	15.2		
BMD Increase >3% at All Three Sites	31.9	1.5		
BMD Increase >6% at All Three Sites	9.2	0.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Total Hip Volumetric BMD as Measured by Quantitative Computed Tomography (QCT) at Month 12

End point title	Percent Change From Baseline in Total Hip Volumetric BMD as Measured by Quantitative Computed Tomography (QCT) at Month 12

End point description:

QCT scans were evaluated by a central imaging laboratory.
Only 2 participants per reporting group had volumetric BMD measured by QCT at baseline and Month 12, therefore, no data is reported here to maintain participant confidentiality.

End point type	Secondary

End point timeframe:

Baseline, Month 12

End point values	Abaloparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[4]	0[5]		
Units: percent change				
arithmetic mean (standard deviation)	()	()		

Notes:

[4] - No data is reported here to maintain participant confidentiality (n=2).

[5] - No data is reported here to maintain participant confidentiality (n=2).

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Femoral Neck Volumetric BMD as Measured by QCT at Month 12

End point title	Percent Change From Baseline in Femoral Neck Volumetric BMD as Measured by QCT at Month 12

End point description:

QCT scans were evaluated by a central imaging laboratory.
Only 2 participants per reporting group had volumetric BMD measured by QCT at baseline and Month 12, therefore, no data is reported here to maintain participant confidentiality

End point type	Secondary

End point timeframe:

Baseline, Month 12

End point values	Abaloparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[6]	0[7]		
Units: percent change				
arithmetic mean (standard deviation)	()	()		

Notes:

[6] - No data is reported here to maintain participant confidentiality (n=2).

[7] - No data is reported here to maintain participant confidentiality (n=2).

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 (after dosing) through Month 13

Adverse event reporting additional description:

Safety Population was used for analyses of treatment-emergent serious and non-serious adverse events that occurred from Day 1 (after dosing) through Month 13. The one death recorded was due to an event that was not treatment-emergent.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants self-administered daily doses of placebo SC 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

Reporting group description:

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

Serious adverse events	Placebo	Abaloparatide	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 79 (5.06%)	8 / 149 (5.37%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung adenocarcinoma			
subjects affected / exposed	0 / 79 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Burns third degree			
subjects affected / exposed	1 / 79 (1.27%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			

subjects affected / exposed	0 / 79 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 79 (1.27%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 79 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	0 / 79 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve prolapse			
subjects affected / exposed	1 / 79 (1.27%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 79 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral nerve palsy			
subjects affected / exposed	0 / 79 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Skin graft rejection			
subjects affected / exposed	1 / 79 (1.27%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	0 / 79 (0.00%)	1 / 149 (0.67%)	
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			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 79 (0.00%)	1 / 149 (0.67%)	
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			
Lumbar spinal stenosis			
subjects affected / exposed	1 / 79 (1.27%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 79 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 79 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Abaloparatide	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 79 (36.71%)	73 / 149 (48.99%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 79 (5.06%)	8 / 149 (5.37%)	
occurrences (all)	4	8	
Nervous system disorders			

Headache			
subjects affected / exposed	4 / 79 (5.06%)	8 / 149 (5.37%)	
occurrences (all)	5	8	
Dizziness			
subjects affected / exposed	1 / 79 (1.27%)	13 / 149 (8.72%)	
occurrences (all)	1	19	
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	4 / 79 (5.06%)	19 / 149 (12.75%)	
occurrences (all)	5	20	
Injection site swelling			
subjects affected / exposed	0 / 79 (0.00%)	10 / 149 (6.71%)	
occurrences (all)	0	10	
Injection site pain			
subjects affected / exposed	0 / 79 (0.00%)	9 / 149 (6.04%)	
occurrences (all)	0	14	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 79 (1.27%)	10 / 149 (6.71%)	
occurrences (all)	1	11	
Back pain			
subjects affected / exposed	5 / 79 (6.33%)	7 / 149 (4.70%)	
occurrences (all)	5	7	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 79 (7.59%)	13 / 149 (8.72%)	
occurrences (all)	7	14	
Bronchitis			
subjects affected / exposed	1 / 79 (1.27%)	8 / 149 (5.37%)	
occurrences (all)	1	8	
Upper respiratory tract infection			
subjects affected / exposed	5 / 79 (6.33%)	7 / 149 (4.70%)	
occurrences (all)	5	7	
Sinusitis			
subjects affected / exposed	4 / 79 (5.06%)	6 / 149 (4.03%)	
occurrences (all)	4	7	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 January 2018	• Information added to present data from the referenced studies to support that there is no difference in serum calcium between men and women and that the 4-hour postdose time point will capture the maximum calcium concentration • For the fixed-sequence testing approach employed to control the Type 1 error at the 2-sided significance level for testing the primary and secondary efficacy endpoints, the significance level was changed from 5% to 1%. In addition, minor editorial changes were also made for consistency/clarity and additional details were provided for SAE reporting requirements.
30 October 2018	• Specified timepoints and endpoints for immunogenicity testing • Added updated PK pharmacokinetics (PK) data • Specified the range of 25-hydroxyvitamin D for inclusion in the study • Changed the timing for retesting of out-of-range laboratory tests • Specified that the exclusion period for participants who have previously received treatment with anabolic steroids or calcineurin inhibitors was within 90 days • Deleted an exclusion criterion that prevented participants from enrolling in the study after receiving anesthesia within 12 weeks.
06 June 2019	• Changed the BMD criteria from a female reference range to the male reference range.
10 December 2019	• Allowed for use a historical height measurement in cases where the height of a participant could not be adequately assessed • Allowed for reflex testing for bone-specific alkaline phosphatase if a participant had an elevated alkaline phosphatase at Screening • Allowed for reflex testing for T3 and free T4 if a participant had thyroid stimulating hormone value outside of the normal range at Screening • Allowed DXA scans within 35 days prior to Screening to be used for determining study eligibility • Clarified when a participant's blood pressure and heart rate at Screening must be reviewed by the Sponsor’s Medical Monitor for determining study eligibility
02 October 2020	• Added sparse PK sampling at the Month 6, 9, and 12 visits In addition, minor editorial changes were also made for consistency/clarity and text was added to clarify that DXA scans were to be performed using a study-approved scanner but could be collected up to 35 days before the participant’s Screening Visit.
30 March 2021	• Revised the efficacy analysis methods (use of a multiple imputation method, specifically a wash-out imputation approach, to impute missing primary endpoint values, and to add clarifications around study procedures, including COVID-19 details) • Clarified several definitions (osteopenia, lost to follow-up, the Safety and Per Protocol Populations) and updated text regarding antibody analyses to align with the planned analysis methods

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

Notes: