Clinical trial results:
Second study on the Effect of Teriparatide on Femoral Neck Fracture Healing

Summary

EudraCT number	2011-001116-65
Trial protocol	HU BE GR PL NL DE
Global end of trial date	20 November 2013

Results information

Result version number	v1 (current)
This version publication date	04 July 2016
First version publication date	02 August 2015

Trial information

Trial identification

Sponsor protocol code	B3D-MC-GHDQ

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01473602
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 14125, Trial Alias: B3D-MC-GHDQ

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877-CTLilly,
Scientific contact	Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877-285-4559,

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	20 November 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 November 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To determine the effect of 6 months of treatment with teriparatide 20 microgram (µg)/day versus placebo on the proportion of men and postmenopausal women ≥50 years of age with successful fracture healing 24 months after internal fixation of a low trauma femoral neck fracture

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 January 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Hungary: 14
Country: Number of subjects enrolled	Romania: 5
Country: Number of subjects enrolled	Korea, Republic of: 9
Country: Number of subjects enrolled	United States: 3
Worldwide total number of subjects	39
EEA total number of subjects	27

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)	9
From 65 to 84 years	26
85 years and over	4

Subject disposition

Recruitment

Recruitment details:

No text entered.

Pre-assignment

Screening details:

No text entered.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Teriparatide

Arm description:

Teriparatide 20 microgram (µg) once-daily by subcutaneous (SC) injection for 6 months. Participants received calcium and vitamin D supplements.
Baseline characteristics values based on number of subjects that received at least 1 dose of study drug.

Arm type	Experimental
Investigational medicinal product name	Teriparatide
Investigational medicinal product code	
Other name	Forteo, Forsteo, LY333334
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

20 microgram (µg) administered once daily by SC injection for 6 months

Investigational medicinal product name	Calcium supplementation
Investigational medicinal product code	
Other name	Dietary Supplement: Calcium supplementation
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The supplement dose for calcium should be up to approximately 1000 milligram (mg)/day elemental calcium starting as soon as possible after screening and continuing through 12 months.

Investigational medicinal product name	Vitamin D supplementation
Investigational medicinal product code	
Other name	Dietary Supplement: Vitamin D supplementation
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

During screening, approximately 1000 International Unit (IU)/day vitamin D. The dose of vitamin D may then be increased at the discretion of the invetigator.

Arm title	Placebo

Arm description:

Placebo once-daily by SC injection for 6 months. Participants received calcium and vitamin D supplements.
Baseline characteristics values based on number of subjects that received at least 1 dose of study drug.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered once daily by subcutaneous (SC) injection for 6 months

Investigational medicinal product name	Calcium supplementation
Investigational medicinal product code	
Other name	Dietary Supplement: Calcium supplementation
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

All participants will receive supplements of calcium and vitamin D beginning at screening and continuing for 12 months.

Investigational medicinal product name	Vitamin D supplementation
Investigational medicinal product code	
Other name	Dietary Supplement: Vitamin D supplementation
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

All participants will receive supplements of calcium and vitamin D beginning at screening and continuing for 12 months.

Number of subjects in period 1	Teriparatide	Placebo
Started	18	21
Received at Least 1 Dose of Study Drug	18	20
Completed 6 Months	12	15
Completed 12 Months	10	13
Completed	10	13
Not completed	8	8
Adverse event, serious fatal	-	1
Consent withdrawn by subject	5	4
Physician decision	1	-
Adverse Event	1	2
Lost to follow-up	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Teriparatide
Reporting group description:	
Teriparatide 20 microgram (µg) once-daily by subcutaneous (SC) injection for 6 months. Participants received calcium and vitamin D supplements. Baseline characteristics values based on number of subjects that received at least 1 dose of study drug.	
Reporting group title	Placebo
Reporting group description:	
Placebo once-daily by SC injection for 6 months. Participants received calcium and vitamin D supplements. Baseline characteristics values based on number of subjects that received at least 1 dose of study drug.	

Reporting group values	Teriparatide	Placebo	Total
Number of subjects	18	21	39
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	73.39	69.93	
standard deviation	± 10.259	± 10.417	-
Gender categorical Units: Subjects			
Female	14	16	30
Male	4	5	9
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	4	5	9
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	14	15	29
More than one race	0	0	0
Unknown or Not Reported	0	1	1
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	1	3
Not Hispanic or Latino	9	9	18
Unknown or Not Reported	7	11	18
Region of Enrollment Units: Subjects			
United States	2	1	3
Hungary	6	8	14
Belgium	2	2	4
Romania	2	3	5
Netherlands	2	2	4
Korea, Republic of	4	5	9

Surgical screw type			
Surgical screws used in initial surgery to repair femur neck hip fracture.			
Units: Subjects			
Cancellous Screws	18	18	36
Sliding Hip Screws	0	2	2
Not Recorded	0	1	1

End points

End points reporting groups

Reporting group title	Teriparatide
Reporting group description:	
Teriparatide 20 microgram (µg) once-daily by subcutaneous (SC) injection for 6 months. Participants received calcium and vitamin D supplements. Baseline characteristics values based on number of subjects that received at least 1 dose of study drug.	
Reporting group title	Placebo
Reporting group description:	
Placebo once-daily by SC injection for 6 months. Participants received calcium and vitamin D supplements. Baseline characteristics values based on number of subjects that received at least 1 dose of study drug.	

Primary: Percentage of Participants With No Revision Surgery at 12 Months After Internal Fixation of a Low-Trauma Femoral Neck Fracture

End point title	Percentage of Participants With No Revision Surgery at 12 Months After Internal Fixation of a Low-Trauma Femoral Neck Fracture
End point description:	
Revision surgery (re-operation) was defined as any additional surgical intervention performed or recommended at the site of the index procedure, except those that were planned at the time of the index procedure.	
End point type	Primary
End point timeframe:	
12 months	

End point values	Teriparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	20		
Units: Percentage of participants				
number (confidence interval 90%)	74 (51 to 88)	93 (70 to 99)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1 for End Point 1
Comparison groups	Teriparatide v Placebo
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.743 [1]
Method	K-M with Greenwood SE
Parameter estimate	Difference in proportion
Point estimate	-0.04

Confidence interval	
level	90 %
sides	1-sided
lower limit	-0.14

Notes:

[1] - P-value is based on Z test statistic with Greenwood estimator for standard errors (SE) to compare two Kaplan-Meier (K-M) estimates at 12 month.

Secondary: Percentage of Participants With Radiographic Evidence of Healing

End point title	Percentage of Participants With Radiographic Evidence of Healing

End point description:

The signs of femoral neck fracture healing and healing complications included disappearance of the fracture line on radiographs. If a participant had radiographic evidence of healing at the 12-month visit, that participant was considered to have radiographic evidence of healing.

Percentage was calculated as: (number of participants with radiographic evidence of healing / total number of participants analyzed) * 100.

End point type	Secondary

End point timeframe:

Randomization, 12 months

End point values	Teriparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	20		
Units: Percentage of participants	56	65		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Pain Control During Ambulation

End point title	Percentage of Participants With Pain Control During Ambulation

End point description:

The worst pain numeric rating scale (NRS) was used to assess the impact of pain on a participant's life. NRS Item 3 assessed the worst musculoskeletal pain severity during the walking test. Pain was measured by an 11-point Likert scale. The following cut-points were used to categorize the NRS responses: 0 = no pain, 1 to 4 = mild pain, 5 to 6 = moderate pain, and 7 to 10 = severe pain. Higher scores indicated more severe pain. Participants with an NRS score of <7 and no worsening of NRS scores >2 from baseline were categorized as having no severe fracture-site pain. Percentage was calculated as: (number of participants with pain control during ambulation / total number of participants analyzed) * 100.

End point type	Secondary

End point timeframe:

12 months

End point values	Teriparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	13		
Units: Percentage of participants	90	100		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Without Severe Fracture-Site Pain During 24 Hours Prior to Visit

End point title	Percentage of Participants Without Severe Fracture-Site Pain During 24 Hours Prior to Visit

End point description:

The NRS was used to assess the impact of pain on a participant's life. Fracture-site pain severity was assessed for pain in the 24 hours preceding a visit. Pain was measured by an 11-point Likert scale. Participants with an NRS score of <7 in the 24 hours preceding a visit and no worsening of NRS score >2 from baseline were categorized as having no severe fracture-site pain. Percentage was calculated as: (number of participants with pain control during 24 hours preceding a visit / total number of participants analyzed) * 100.

End point type	Secondary

End point timeframe:

12 months

End point values	Teriparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	14		
Units: Percentage of participants	82	93		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Without Severe Fracture-Site Pain During Weight Bearing

End point title	Percentage of Participants Without Severe Fracture-Site Pain During Weight Bearing

End point description:

The worst pain NRS was used to assess the impact of pain on a participant's life. Fracture-site pain severity was assessed for pain on weight bearing. Pain was measured by an 11-point Likert scale. Participants with an NRS score of <7 during weight bearing and no worsening of NRS score >2 from baseline were categorized as having no severe fracture-site pain. Percentage was calculated as: (number of participants with pain control during weight bearing / total number of participants) * 100.

End point type	Secondary

End point timeframe:

12 months

End point values	Teriparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	13		
Units: Percentage of participants	91	85		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Functional Evidence of Healing

End point title	Percentage of Participants With Functional Evidence of Healing

End point description:

Functional healing was defined as ability to walk with a gait speed ≥ 0.05 meters/second (m/s) with a change from baseline ≥ -0.1 m/s. The walking test involved having the participant walk a distance of 7 meters (m) at a self-selected, comfortable pace. A 4-m portion of the test was timed to determine the participant's gait speed in m/s.

Percentage was calculated as: (number of participants with functional evidence of healing / total number of participants analyzed) * 100.

End point type	Secondary

End point timeframe:

12 Months

End point values	Teriparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	15		
Units: Percentage of participants	77	67		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Able to Ambulate

End point title	Percentage of Participants Able to Ambulate

End point description:

Ability to ambulate was defined as ambulatory with or without convalescent aid. Percentage was calculated as: (number of participants able to ambulate / total number of participants analyzed) * 100.

End point type	Secondary

End point timeframe:

12 months

End point values	Teriparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	15		
Units: Percentage of participants	77	93		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Regained Their Prefracture Ambulatory Status

End point title	Percentage of Participants Who Regained Their Prefracture Ambulatory Status

End point description:

Prefracture ambulatory status was defined as either ambulatory with or without a walking aid. A participant was considered to have regained their prefracture ambulatory status if the participant's postsurgery ambulatory status was returned to or was improved from their pre-surgery ambulatory status. Percentage was calculated as = (number of participants who regained their ambulatory status / total number of participants analyzed) *100.

End point type	Secondary

End point timeframe:

12 months

End point values	Teriparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	15		
Units: Percentage of participants	47	63		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline to 6 Months in Worst Fracture-Site Pain

End point title	Mean Change From Baseline to 6 Months in Worst Fracture-Site Pain

End point description:

The worst pain NRS was used to assess the impact of pain on a participant's life. Participants with an NRS score of <7 were categorized as having no severe fracture-site pain. Least squares (LS) means was calculated using analysis of covariance (ANCOVA) adjusted for baseline, treatment group, region, fracture type, and fixation type.

End point type	Secondary

End point timeframe:

Baseline, 6 Months

End point values	Teriparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	20		
Units: Units on a scale				
least squares mean (standard error)				
During ambulation (n= 10, 13)	-1.6 (± 1.46)	-1.3 (± 1.45)		
During 24 hours preceding visit (n= 10, 14)	-1.2 (± 1.27)	-1.4 (± 1.21)		
On weight bearing (n= 10, 13)	-2 (± 1.5)	-1.4 (± 1.45)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline to 6 Months in Gait Speed

End point title	Mean Change From Baseline to 6 Months in Gait Speed

End point description:

The walking test involved having the participant walk a distance of 7 m at a self-selected, comfortable pace. A 4-m portion of the test was timed to determine the participant’s gait speed in m/s. LS means was calculated using ANCOVA adjusted for baseline, treatment group, region, fracture type, and fixation type

End point type	Secondary

End point timeframe:

Baseline, 6 Months

End point values	Teriparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	13		
Units: m/s				
least squares mean (standard error)	0.168 (± 0.153)	0.118 (± 0.145)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Revision Surgery

End point title	Time to Revision Surgery

End point description:

Time to revision surgery was defined as the time from initial hip fracture surgery to revision surgery, or recommendation for revision surgery if recommended but not performed. Time to revision surgery was censored at the date of the last contact.

End point type	Secondary

End point timeframe:

Baseline, Revision Surgery

End point values	Teriparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	20		
Units: Days				
median (full range (min-max))	333.5 (35 to 443)	361 (29 to 426)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline to 6 Months on Short Form-12 (SF-12) Physical (PCS) and Mental Component Summary (MCS) Scores

End point title	Mean Change From Baseline to 6 Months on Short Form-12 (SF-12) Physical (PCS) and Mental Component Summary (MCS) Scores

End point description:

SF-12 is a self-reported questionnaire covering a mental component score (MCS) and a physical component score (PCS), each scoring from a 0 to 100 (worst to best) scale. LS means was calculated using ANCOVA adjusted for baseline, treatment group, region, fracture type, fixation type, visit, and visit-by-treatment interaction.

End point type	Secondary

End point timeframe:

Baseline, 6 Months

End point values	Teriparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	20		
Units: Units on a scale				
least squares mean (standard error)				
PCS Month 6 (n=12, 14) MCS Month 6 (n=12, 14)	0.89 (± 3) -8.84 (± 5.8)	1.78 (± 2.75) -10.71 (± 5.14)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline to 6 Months on Western Ontario McMaster Osteoarthritis Index (WOMAC)

End point title	Mean Change From Baseline to 6 Months on Western Ontario McMaster Osteoarthritis Index (WOMAC)

End point description:

WOMAC: was a self-reported questionnaire that consisted of 24 questions covering 3 health domains: Pain (5 items: during walking, using stairs, in bed, sitting or lying, and standing), Stiffness (2 items: after first waking and later in the day), and Physical Function. Each domain was scored by summing the individual items and transforming the scores into a 0 to 100 (best to worst) scale. Lower scores indicated better health status or functioning. LS means was calculated using ANCOVA adjusted for baseline, treatment group, region, fracture type, fixation type, visit, and visit-by-treatment interaction.

End point type	Secondary

End point timeframe:

Baseline, 6 Months

End point values	Teriparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	20		
Units: Units on a scale				
least squares mean (standard error)				
Physical Function Score - Month 6 (n=11, 12)	10.5 (± 12.41)	1.1 (± 12.42)		
Pain Score - Month 6 (n=12, 13)	10.6 (± 10.64)	13.6 (± 10.09)		
Stiffness Score - Month 6 (n=12, 15)	13.5 (± 8.71)	16.9 (± 7.74)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline to 6 Months on European Quality of Life Questionnaire (EQ-5D) Overall Health Score

End point title	Mean Change From Baseline to 6 Months on European Quality of Life Questionnaire (EQ-5D) Overall Health Score

End point description:

The EQ-5D is a 5-item, self-reported, generic, multidimensional, health-related, quality-of-life instrument with 5 items. Overall health state score was also self-reported using a visual analogue scale (VAS) marked on a scale scored from 0 (worst imaginable health state) to 100 (best imaginable health state). Higher scores represented better health state with 0 representing worst imaginable health state and 100 representing best imaginable health state. LS means was calculated using ANCOVA adjusted for baseline, treatment group, region.

End point type	Secondary

End point timeframe:

Baseline, 6 Months

End point values	Teriparatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	20		
Units: Units on a scale				
least squares mean (standard error)	13 (± 6.42)	10.4 (± 6.67)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Entire Study	
Adverse event reporting additional description:	
B3D-MC-GHDQ	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	Screening
Reporting group description: -	
Reporting group title	Placebo Acute
Reporting group description: -	
Reporting group title	Teriparatide 20 mcg Acute
Reporting group description: -	
Reporting group title	Placebo Follow-up
Reporting group description: -	
Reporting group title	Teriparatide 20 mcg Follow-up
Reporting group description: -	

Serious adverse events	Screening	Placebo Acute	Teriparatide 20 mcg Acute
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 39 (2.56%)	2 / 20 (10.00%)	1 / 18 (5.56%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
blood glucose fluctuation			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	0 / 20 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
fall			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	1 / 20 (5.00%)	0 / 18 (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

femur fracture			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	1 / 20 (5.00%)	0 / 18 (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 myocardial infarction			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
myocardial infarction			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 39 (2.56%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
hyperventilation			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 39 (2.56%)	0 / 20 (0.00%)	0 / 18 (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
Skin and subcutaneous tissue disorders			
erythema multiforme			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	1 / 20 (5.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations			
bronchopneumonia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
osteomyelitis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	1 / 20 (5.00%)	0 / 18 (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
Metabolism and nutrition disorders			
hyperglycaemia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo Follow-up	Teriparatide 20 mcg Follow-up	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 15 (13.33%)	1 / 12 (8.33%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
blood glucose fluctuation			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 12 (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			
fall			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

femur fracture			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
acute myocardial infarction			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 15 (6.67%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
myocardial infarction			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 15 (6.67%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 12 (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			
hyperventilation			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
erythema multiforme			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 12 (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			
bronchopneumonia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
osteomyelitis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
hyperglycaemia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	1 / 12 (8.33%)	
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: 1 %

Non-serious adverse events	Screening	Placebo Acute	Teriparatide 20 mcg Acute
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 39 (12.82%)	5 / 20 (25.00%)	3 / 18 (16.67%)
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 39 (2.56%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
hypotension			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
orthostatic hypotension			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	0 / 39 (0.00%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
bladder catheterisation			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	1 / 20 (5.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
coronary arterial stent insertion			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
removal of internal fixation			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
wisdom teeth removal			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	1 / 20 (5.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
wrist surgery			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
fatigue			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	0 / 20 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
pulmonary embolism			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	1 / 20 (5.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			

depression			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
sleep disorder			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	1 / 20 (5.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Investigations			
blood cholesterol increased			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	1 / 20 (5.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
bone density decreased			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
headache			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 39 (2.56%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
lethargy			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	1 / 20 (5.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
multiple system atrophy			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
parkinsonism			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
sciatica			

alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	1 / 20 (5.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
vascular dementia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 39 (2.56%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
hyperchlorhydria			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	0 / 20 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
nausea			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 39 (2.56%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
toothache			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	1 / 20 (5.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
vomiting			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
rash			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 39 (2.56%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
skin necrosis			

alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	1 / 20 (5.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	0 / 20 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
fracture pain			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 39 (2.56%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
osteopenia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 39 (2.56%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
pain in extremity			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	1 / 20 (5.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
pharyngitis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
vulvovaginal candidiasis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed[1]	0 / 30 (0.00%)	1 / 16 (6.25%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
hyperlipidaemia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 39 (0.00%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Placebo Follow-up	Teriparatide 20 mcg Follow-up	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 15 (26.67%)	3 / 12 (25.00%)	
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
hypotension			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
orthostatic hypotension			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Surgical and medical procedures			
bladder catheterisation			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
coronary arterial stent insertion			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 15 (6.67%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
removal of internal fixation			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
wisdom teeth removal			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
wrist surgery			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	1 / 15 (6.67%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
fatigue			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
pulmonary embolism			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
depression			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 15 (6.67%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
sleep disorder			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Investigations			
blood cholesterol increased			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
bone density decreased			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 15 (6.67%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
headache			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	

lethargy			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
multiple system atrophy			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
parkinsonism			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
sciatica			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 15 (6.67%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
vascular dementia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 15 (6.67%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
hyperchlorhydria			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
nausea			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
toothache			

alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
vomiting			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 15 (6.67%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
rash			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
skin necrosis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
fracture pain			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
osteopenia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
pain in extremity			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 15 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			

pharyngitis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 15 (6.67%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
vulvovaginal candidiasis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed[1]	0 / 12 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
hyperlipidaemia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 15 (6.67%)	0 / 12 (0.00%)	
occurrences (all)	1	0	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 December 2012	The sponsor decided to end enrolment prematurely. The decision to stop enrolment was due to operational challenges and enrolment feasibility with regard to completing the study in a timely manner and not based on any safety or efficacy concerns in the trial. All active patients who were enrolled were offered to continue, and complete the study to 12 months.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported