



Clinical trial results: Teriparatide (Forsteo) Treatment in Postmenopausal Women: Mechanism of Action. A two year open label single arm study of teriparatide in secondary care.

Summary

EudraCT number	2010-021009-19
Trial protocol	GB
Global end of trial date	21 August 2015

Results information

Result version number	v1 (current)
This version publication date	28 July 2019
First version publication date	28 July 2019

Trial information

Trial identification

Sponsor protocol code	STH15466
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01293292
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sheffield Teaching Hospitals NHS Foundation Trust
Sponsor organisation address	Trust Headquarters, 8 Beech Hill Road, Sheffield, United Kingdom, S10 2SB
Public contact	Dr Dipak Patel, Sheffield Teaching Hospitals NHS Foundation Trust, ResearchAdministration@sth.nhs.uk
Scientific contact	Dr Dipak Patel, Sheffield Teaching Hospitals NHS Foundation Trust, ResearchAdministration@sth.nhs.uk

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	11 January 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 December 2014
Global end of trial reached?	Yes
Global end of trial date	21 August 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objectives of the trial were to develop a strategy for evaluating the efficacy of anabolic therapies by:

1. Fully describing the changes in bone turnover using biochemical markers in response to anabolic therapy by: a) biochemical marker type, b) time
2. Fully describing the changes in BMD in response to anabolic therapy by: a) site, b) bone compartment, c) time

Protection of trial subjects:

All participants were given a participant information sheet to read and consider for at least 24 hours before attending for a screening visit for the study. Participants were reviewed by a clinician, or an experienced study nurse who was delegated to this task, according to the strict inclusion and exclusion criteria. All participants give written informed consent prior to enrolment to the study. All subjects received a standard and licensed treatment for osteoporosis. Subjects were required to attend for the study visits, detailed in the study schedule, to give blood and urine samples and have DXA, HR-pQCT and QCT measurements. The volume of blood required from the study subjects was up to approximately 50 mL for the screening visit and up to approximately 25mL for the subsequent visits, the total volume of blood taken was approximately 300mL over the study period.

An assessment of radiation exposure was performed by the Radiation Protection Advisor for the Sheffield Teaching Hospitals NHS Foundation Trust prior to ethical review of the project. GCP procedures were in place to ensure appropriate consent, confidentiality and privacy. Data were handled in accordance with the Data Protection Act 1998. There are no issues concerning racial and cultural diversity as we did not exclude subjects based on these criteria.

Subjects received a payment to compensate for time and inconvenience.

Background therapy:

To ensure that all study participants were vitamin D replete prior to administration of the teriparatide, a 100,000 IU cholecalciferol (vitamin D3) load was given orally at the end of the screening visit (-63 ± 28 days from baseline). A blood sample to assess the serum 25-hydroxyvitamin D level was then taken at baseline. If the results of the blood test revealed a serum 25-hydroxyvitamin D level <50 nmol/L, then a second loading dose was given at an extra study visit and a further blood sample was taken to assess serum 25-hydroxyvitamin D levels. A total of three 100,000 IU cholecalciferol loads were administered per individual, if required. Further 100,000 IU cholecalciferol loads were administered at six-monthly intervals throughout the study (weeks 26, 52 and 78) to ensure that all study participants remained replete.

In keeping with usual clinical practice all participants also received daily calcium (600mg) and vitamin D3 (400IU) supplements as Adcal D3 (Prostrakan: Galashiels, UK) throughout the study.

Evidence for comparator:

Single arm. No comparators were used

Actual start date of recruitment	08 February 2011
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 Kingdom: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

We identified women with postmenopausal osteoporosis from Sheffield metabolic bone clinics, general practitioner (GP) referrals for bone densitometry and via GP mail-outs. Former research participants, who had consented to participate in future research projects, were also approached.

Pre-assignment

Screening details:

We enrolled women >5 years postmenopausal but aged <85 years, ambulatory, serum 25-hydroxyvitamin D >50 nmol/L, willing and able to give informed consent. Exclusion criteria included ongoing conditions or diseases known to cause abnormalities of calcium metabolism or skeletal health, morbid obesity and fracture in the past year.

Period 1

Period 1 title	Overall trial (104 weeks) (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Not blinded. All participants received the same treatment

Arms

Are arms mutually exclusive?	No
Arm title	Teriparatide treatment

Arm description:

The study drug was teriparatide (Forsteo 20 mcg daily: Eli Lilly and Company, Basingstoke, UK). Participants received 104 weeks of teriparatide treatment delivered by a daily self-administered subcutaneous injection in the thigh or abdomen. The drug was supplied in pre-filled pens which administered 20 mcg doses. All participants were trained in correct injection technique.

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

Dosage and administration details:

Forsteo is a recombinant human parathyroid hormone analog (1-34), [rhPTH (1-34)] indicated for treatment of (i) osteoporosis in postmenopausal women and in men at increased risk of fracture, and (ii) osteoporosis associated with sustained systemic glucocorticoid therapy in women and men at increased risk of fracture.

The recommended dose is 20 mcg subcutaneously once daily. Presentation is as 2.4ml pre-filled pens containing a solution of 600 micrograms of teriparatide (250 micrograms per ml) for injection. Each pen contains 28 doses of 20micrograms/80 microliters of teriparatide. This is administered as a subcutaneous injection into the thigh or abdominal wall. Use of the drug for more than 2 years during a patient's lifetime is not recommended.

Arm title	Baseline pre-treatment
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Arm description:

Pre-treatment as advised in guidance dated - EudraCT FAQ v1.4 May 2019:

Currently the system cannot accommodate this specific scenario. Hence, you can proceed with a workaround whereby the baseline is considered one group and the end data another group.

By doing that you will be able to use the statistical analysis set to report analysis for a single arm.

Arm type	Baseline
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No investigational medicinal product assigned in this arm

Number of subjects in period 1	Teriparatide treatment	Baseline pre-treatment
Started	20	20
Completed	16	16
Not completed	4	4
Lost to follow-up	4	4

Baseline characteristics

Reporting groups

Reporting group title	Overall trial (104 weeks)
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Reporting group description: -

Reporting group values	Overall trial (104 weeks)	Total	
Number of subjects	20	20	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	9	9	
From 65-84 years	11	11	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	65.4		
standard deviation	± 5.5	-	
Gender categorical			
Postmenopausal women (n = 20, ages 65.4 ± 5.5 years) with osteoporosis, defined as an areal BMD (aBMD) T score < -2.5 at the lumbar spine or proximal femur, were enrolled into the study. We identified women with postmenopausal osteoporosis from Sheffield metabolic bone clinics, general practitioner (GP) referrals for bone densitometry and via GP mail-outs. Former research participants, who had consented to participate in future research projects, were also approached.			
Units: Subjects			
Female	20	20	
Male	0	0	
Height			
Units: cm			
arithmetic mean	161		
standard deviation	± 4	-	
Weight			
Units: kg			
arithmetic mean	64		
standard deviation	± 8.1	-	
Lumbar spine aBMD T-score			
Units: n/a			
arithmetic mean	-2.8		
standard deviation	± 0.3	-	
Total proximal femur aBMD T-score			
Units: n/a			
arithmetic mean	-2.2		
standard deviation	± 0.5	-	

femoral neck aBMD T-score			
Units: n/a			
arithmetic mean	-1.5		
standard deviation	± 0.6	-	

Subject analysis sets

Subject analysis set title	Study completers
Subject analysis set type	Per protocol

Subject analysis set description:

We performed per-protocol analyses which only used data acquired from those participants who attended for all study visits, adhered to all study procedures and demonstrated $\geq 75\%$ compliance with study medication; referred to as completers. A medication compliance threshold of 75% was chosen as it equated approximately to 5 injections of teriparatide per week.

Subject analysis set title	All enrolled
Subject analysis set type	Full analysis

Subject analysis set description:

Every participant that was enrolled into trial

Reporting group values	Study completers	All enrolled	
Number of subjects	16	20	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	8	9	
From 65-84 years	8	11	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	65.4		
standard deviation	± 5.5	±	
Gender categorical			
Postmenopausal women (n = 20, ages 65.4 ± 5.5 years) with osteoporosis, defined as an areal BMD (aBMD) T score < -2.5 at the lumbar spine or proximal femur, were enrolled into the study. We identified women with postmenopausal osteoporosis from Sheffield metabolic bone clinics, general practitioner (GP) referrals for bone densitometry and via GP mail-outs. Former research participants, who had consented to participate in future research projects, were also approached.			
Units: Subjects			
Female	16		
Male			
Height			
Units: cm			
arithmetic mean	162		
standard deviation	± 3	±	
Weight			
Units: kg			
arithmetic mean	64		

standard deviation	± 9	$\pm$	
Lumbar spine aBMD T-score			
Units: n/a			
arithmetic mean	-2.8		
standard deviation	± 0.2	$\pm$	
Total proximal femur aBMD T-score			
Units: n/a			
arithmetic mean	-1.5		
standard deviation	± 0.7	$\pm$	
femoral neck aBMD T-score			
Units: n/a			
arithmetic mean	-2.1		
standard deviation	± 0.5	$\pm$	

End points

End points reporting groups

Reporting group title	Teriparatide treatment
Reporting group description: The study drug was teriparatide (Forsteo 20 mcg daily: Eli Lilly and Company, Basingstoke, UK). Participants received 104 weeks of teriparatide treatment delivered by a daily self-administered subcutaneous injection in the thigh or abdomen. The drug was supplied in pre-filled pens which administered 20 mcg doses. All participants were trained in correct injection technique.	
Reporting group title	Baseline pre-treatment
Reporting group description: Pre-treatment as advised in guidance dated - EudraCT FAQ v1.4 May 2019: Currently the system cannot accommodate this specific scenario. Hence, you can proceed with a workaround whereby the baseline is considered one group and the end data another group. By doing that you will be able to use the statistical analysis set to report analysis for a single arm.	
Subject analysis set title	Study completers
Subject analysis set type	Per protocol
Subject analysis set description: We performed per-protocol analyses which only used data acquired from those participants who attended for all study visits, adhered to all study procedures and demonstrated $\geq 75\%$ compliance with study medication; referred to as completers. A medication compliance threshold of 75% was chosen as it equated approximately to 5 injections of teriparatide per week.	
Subject analysis set title	All enrolled
Subject analysis set type	Full analysis
Subject analysis set description: Every participant that was enrolled into trial	

Primary: Percent change in L1-L3 trabecular volumetric bone mineral density (vBMD)

End point title	Percent change in L1-L3 trabecular volumetric bone mineral density (vBMD)
End point description:	
End point type	Primary
End point timeframe: Baseline to 104 weeks	

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[1]	
Units: percent				
arithmetic mean (standard error)	28.5 ($\pm$ 19.4)	0 ($\pm$ 0)	28.5 ($\pm$ 19.4)	

Notes:

[1] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in L1-L3 trabecular vBMD
Statistical analysis description: Percent change in L1-L3 trabecular vBMD from baseline to week 104	

Comparison groups	Teriparatide treatment v Baseline pre-treatment
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	28.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.2
upper limit	38.8
Variability estimate	Standard deviation
Dispersion value	19.4

Secondary: Percent change in total body areal bone mineral content (aBMC)

End point title	Percent change in total body areal bone mineral content (aBMC)
End point description:	Percent change in total body aBMC between baseline and week 104
End point type	Secondary
End point timeframe:	Baseline to week 104

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[2]	
Units: percent				
arithmetic mean (standard error)	-1.17 (± 0.94)	0 (± 0)	-1.17 (± 0.94)	

Notes:

[2] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in total body aBMC
Statistical analysis description:	Percent change in total body aBMC between baseline and week 104
Comparison groups	Teriparatide treatment v Baseline pre-treatment

Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.17
upper limit	0.84
Variability estimate	Standard error of the mean
Dispersion value	0.94

Secondary: Percent change in sub-total body areal bone mineral content (aBMC)

End point title	Percent change in sub-total body areal bone mineral content (aBMC)
End point description:	Percent change in sub-total body aBMC between baseline and week 104. Sub-total body aBMC = total body aBMC minus skull aBMC.
End point type	Secondary
End point timeframe:	
Baseline to week 104	

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[3]	
Units: percent				
arithmetic mean (standard error)	-0.04 (± 0.90)	0 (± 0)	-0.04 (± 0.90)	

Notes:

[3] - Per-protocol analysis of completers

Statistical analyses

Statistical analysis title	Percent change in sub-total body aBMC
Statistical analysis description:	
Percent change in sub-total body aBMC between baseline and week 104	
Comparison groups	Baseline pre-treatment v Teriparatide treatment
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.04

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.96
upper limit	1.88
Variability estimate	Standard error of the mean
Dispersion value	0.9

Secondary: Percent change in skull areal bone mineral content (aBMC)

End point title	Percent change in skull areal bone mineral content (aBMC)
End point description:	
Percent change in skull aBMC between baseline and week 104	
End point type	Secondary
End point timeframe:	
Baseline to week 104	

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[4]	
Units: percent				
arithmetic mean (standard error)	-4.96 (± 1.87)	0 (± 0)	-4.96 (± 1.87)	

Notes:

[4] - Per-protocol analysis of completers

Statistical analyses

Statistical analysis title	Percent change in skull aBMC
Statistical analysis description:	
Percent change in skull aBMC between baseline and week 104	
Comparison groups	Baseline pre-treatment v Teriparatide treatment
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.02
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-4.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.94
upper limit	-0.98
Variability estimate	Standard error of the mean
Dispersion value	1.87

Secondary: Percent change in arms areal bone mineral density (aBMC)

End point title	Percent change in arms areal bone mineral density (aBMC)
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End point description:

Percent change in arms aBMC between baseline and week 104

End point type	Secondary
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End point timeframe:

Baseline to week 104

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[5]	
Units: percent				
arithmetic mean (standard error)	-5.12 (± 1.08)	0 (± 0)	-5.12 (± 1.08)	

Notes:

[5] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in arms aBMC
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Statistical analysis description:

Percentage change in arms aBMC between baseline and week 104

Comparison groups	Baseline pre-treatment v Teriparatide treatment
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0003
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-5.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.43
upper limit	-2.81
Variability estimate	Standard error of the mean
Dispersion value	1.08

Secondary: Percent change in thoracic spine areal bone mineral content (aBMC)

End point title	Percent change in thoracic spine areal bone mineral content (aBMC)
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End point description:

Percent change in thoracic spine aBMC from baseline to week 104

End point type	Secondary
End point timeframe:	
Baseline to week 104	

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[6]	
Units: percent				
arithmetic mean (standard error)	7.20 (± 3.97)	0 (± 0)	7.20 (± 3.97)	

Notes:

[6] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in thoracic spine aBMC
Statistical analysis description:	
Percentage change in thoracic spine aBMC between baseline and week 104	
Comparison groups	Teriparatide treatment v Baseline pre-treatment
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.09
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	7.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.26
upper limit	15.67
Variability estimate	Standard error of the mean
Dispersion value	3.97

Secondary: Percent change in lumbar spine areal bone mineral content (aBMC)

End point title	Percent change in lumbar spine areal bone mineral content (aBMC)
End point description:	
Percent change in lumbar spine aBMC between baseline and week 104	
End point type	Secondary
End point timeframe:	
Baseline to week 104	

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[7]	
Units: percent				
arithmetic mean (standard error)	23.49 (± 4.34)	0 (± 0)	23.49 (± 4.34)	

Notes:

[7] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in lumbar spine aBMC
Statistical analysis description:	
Percent change in lumbar spine aBMC between baseline and week 104	
Comparison groups	Teriparatide treatment v Baseline pre-treatment
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	23.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.24
upper limit	32.74
Variability estimate	Standard error of the mean
Dispersion value	4.34

Secondary: Percent change in ribs areal bone mineral content (aBMC)

End point title	Percent change in ribs areal bone mineral content (aBMC)
End point description:	
Percent change in ribs aBMC between baseline and week 104	
End point type	Secondary
End point timeframe:	
Baseline to week 104	

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[8]	
Units: percent				
arithmetic mean (standard error)	3.07 (± 3.42)	0 (± 0)	3.07 (± 3.42)	

Notes:

[8] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in ribs aBMC
Statistical analysis description:	
Percent change in ribs aBMC between baseline and week 104	
Comparison groups	Teriparatide treatment v Baseline pre-treatment
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	3.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.24
upper limit	10.37
Variability estimate	Standard error of the mean
Dispersion value	3.42

Secondary: Percent change in pelvis areal bone mineral content (aBMC)

End point title	Percent change in pelvis areal bone mineral content (aBMC)
End point description:	
Percent change in pelvis aBMC between baseline and week 104	
End point type	Secondary
End point timeframe:	
Baseline to week 104	

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[9]	
Units: percent				
arithmetic mean (standard error)	9.29 (± 2.09)	0 (± 0)	9.29 (± 2.09)	

Notes:

[9] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in pelvis aBMC
Statistical analysis description:	
Percent change in pelvis aBMC between baseline and week 104	
Comparison groups	Baseline pre-treatment v Teriparatide treatment v Study completers
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0005
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	9.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.38
upper limit	13.75
Variability estimate	Standard error of the mean
Dispersion value	2.09

Secondary: Percent change in legs areal bone mineral content (aBMC)

End point title	Percent change in legs areal bone mineral content (aBMC)
End point description:	
Percent change in legs aBMC between baseline and week 104	
End point type	Secondary
End point timeframe:	
Baseline to week 104	

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[10]	
Units: percent				
arithmetic mean (standard error)	-2.94 (± 1.07)	0 (± 0)	-2.94 (± 1.07)	

Notes:

[10] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in legs aBMC
Statistical analysis description:	
Percent change in legs aBMC between baseline and week 104	
Comparison groups	Teriparatide treatment v Baseline pre-treatment

Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.01
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-2.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.21
upper limit	-0.67
Variability estimate	Standard error of the mean
Dispersion value	1.07

Secondary: Percent change in central total body areal bone mineral content (aBMC)

End point title	Percent change in central total body areal bone mineral content (aBMC)
End point description:	Percent change in central total body aBMC including ribs, pelvis, thoracic spine and lumbar spine.
End point type	Secondary
End point timeframe:	
Baseline to week 104	

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[11]	
Units: percent				
arithmetic mean (standard error)	8.52 (± 1.57)	0 (± 0)	8.52 (± 1.57)	

Notes:

[11] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in central total body aBMC
Statistical analysis description:	
Percent change in central total body aBMC between baseline and week 104	
Comparison groups	Baseline pre-treatment v Teriparatide treatment
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	8.52

Confidence interval	
level	95 %
sides	2-sided
lower limit	5.16
upper limit	11.87
Variability estimate	Standard error of the mean
Dispersion value	1.57

Secondary: Percent change in peripheral total body areal bone mineral content (aBMC)

End point title	Percent change in peripheral total body areal bone mineral content (aBMC)
End point description: Percent change in peripheral total body aBMC. This includes arms, legs and skull aBMC.	
End point type	Secondary
End point timeframe: Baseline to week 104	

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[12]	
Units: percent				
arithmetic mean (standard error)	-4.09 (± 1.08)	0 (± 0)	-4.09 (± 1.08)	

Notes:

[12] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in peripheral total body aBMC
Statistical analysis description: Percent change in peripheral total body aBMC between baseline and week 104	
Comparison groups	Teriparatide treatment v Baseline pre-treatment
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.002
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-4.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.39
upper limit	-1.79
Variability estimate	Standard error of the mean
Dispersion value	1.08

Secondary: Percent change in total lumbar spine areal bone mineral density (aBMD)

End point title	Percent change in total lumbar spine areal bone mineral density (aBMD)
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End point description:

Percent change in total lumbar spine aBMD between baseline and week 104

End point type	Secondary
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End point timeframe:

Baseline to week 104

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[13]	
Units: percent				
arithmetic mean (standard deviation)	11.8 (± 5.8)	0 (± 0)	11.8 (± 5.8)	

Notes:

[13] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in total lumbar spine aBMD
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Statistical analysis description:

Percent change in total lumbar spine aBMD between baseline and week 104

Comparison groups	Teriparatide treatment v Baseline pre-treatment
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Number of subjects included in analysis	32
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Analysis specification	Pre-specified
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Analysis type	other
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P-value	< 0.0001
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Method	ANCOVA
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Parameter estimate	Mean difference (final values)
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Point estimate	11.8
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Confidence interval

level	95 %
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sides	2-sided
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lower limit	8.7
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upper limit	14.9
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Variability estimate	Standard deviation
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Dispersion value	5.8
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Secondary: Percent change in radius total volumetric bone mineral density (vBMD)

End point title	Percent change in radius total volumetric bone mineral density (vBMD)
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End point description:	
Percentage change in radius total vBMD between baseline and week 104	
End point type	Secondary
End point timeframe:	
Baseline to week 104	

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[14]	
Units: percent				
arithmetic mean (standard deviation)	-2.8 (± 6.7)	0 (± 0)	-2.8 (± 6.7)	

Notes:

[14] - Pre-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in radius total vBMD
Statistical analysis description:	
Percent change in radius total vBMD between baseline and week 104	
Comparison groups	Baseline pre-treatment v Teriparatide treatment
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.03
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.4
upper limit	0.8
Variability estimate	Standard deviation
Dispersion value	6.7

Secondary: Percent change in tibia total volumetric bone mineral density (vBMD)

End point title	Percent change in tibia total volumetric bone mineral density (vBMD)
End point description:	
Percent change in tibia total (vBMD) between baseline and week 104	
End point type	Secondary
End point timeframe:	
Baseline to 104 weeks	

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[15]	
Units: percent				
arithmetic mean (standard deviation)	-2.5 (± 5.5)	0 (± 0)	-2.5 (± 5.5)	

Notes:

[15] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in tibia total vBMD
Statistical analysis description:	
Percent change in tibia total vBMD between baseline and week 104	
Comparison groups	Teriparatide treatment v Baseline pre-treatment
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.008
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.4
upper limit	0.4
Variability estimate	Standard deviation
Dispersion value	5.5

Secondary: Percent change in tibia trabecular volumetric bone mineral density (vBMD)

End point title	Percent change in tibia trabecular volumetric bone mineral density (vBMD)
End point description:	
Percent change in tibia trabecular vBMD between baseline and week 104	
End point type	Secondary
End point timeframe:	
Baseline to week 104	

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[16]	
Units: percent				
arithmetic mean (standard deviation)	-1.4 (± 6.4)	0 (± 0)	-1.4 (± 6.4)	

Notes:

[16] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in tibia trabecular vBMD
Statistical analysis description:	
Percent change in tibia trabecular vBMD between baseline and week 104	
Comparison groups	Baseline pre-treatment v Teriparatide treatment
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	2
Variability estimate	Standard deviation
Dispersion value	6.4

Secondary: Percent change in radius trabecular number

End point title	Percent change in radius trabecular number
End point description:	
Percent change in radius trabecular number between baseline and week 104	
End point type	Secondary
End point timeframe:	
Baseline to week 104	

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[17]	
Units: percent				
arithmetic mean (standard deviation)	-3.5 (± 7.6)	0 (± 0)	-3.5 (± 7.6)	

Notes:

[17] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in radius trabecular number
Statistical analysis description:	
Percent change in radius trabecular number between baseline and week 104	
Comparison groups	Baseline pre-treatment v Teriparatide treatment
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-3.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.5
upper limit	0.5
Variability estimate	Standard deviation
Dispersion value	7.6

Secondary: Percent change in tibia trabecular number

End point title	Percent change in tibia trabecular number
End point description:	
Percent change in tibia trabecular number between baseline and week 104	
End point type	Secondary
End point timeframe:	
Baseline to week 104	

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[18]	
Units: percent				
arithmetic mean (standard deviation)	-1.0 (± 9.3)	0 (± 0)	-1.0 (± 9.3)	

Notes:

[18] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in tibia trabecular number
Statistical analysis description:	
Percent change in tibia trabecular number between baseline and week 104	
Comparison groups	Teriparatide treatment v Baseline pre-treatment
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.06
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6
upper limit	4
Variability estimate	Standard deviation
Dispersion value	9.3

Secondary: Percent change in radius trabecular thickness

End point title	Percent change in radius trabecular thickness
End point description:	
Percent change in radius trabecular thickness between baseline and week 104	
End point type	Secondary
End point timeframe:	
Baseline to week 104	

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[19]	
Units: percent				
arithmetic mean (standard deviation)	2.7 (± 8.0)	0 (± 0)	2.7 (± 8.0)	

Notes:

[19] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in radius trabecular thickness
Statistical analysis description:	
Percent change in radius trabecular thickness between baseline and week 104	
Comparison groups	Baseline pre-treatment v Teriparatide treatment

Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	7
Variability estimate	Standard deviation
Dispersion value	8

Secondary: Percent change in tibia trabecular thickness

End point title	Percent change in tibia trabecular thickness
End point description:	Percent change in tibia trabecular thickness between baseline and week 104
End point type	Secondary
End point timeframe:	Baseline to week 104

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[20]	
Units: percent				
arithmetic mean (standard deviation)	-0.2 (± 9.2)	0 (± 0)	-0.2 (± 9.2)	

Notes:

[20] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in tibia trabecular thickness
Statistical analysis description:	Percent change in tibia trabecular thickness between baseline and week 104
Comparison groups	Teriparatide treatment v Baseline pre-treatment
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.05
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.1
upper limit	4.7
Variability estimate	Standard deviation
Dispersion value	9.2

Secondary: Percent change in radius trabecular separation

End point title	Percent change in radius trabecular separation
End point description: Percent change in radius trabecular separation between baseline and week 104	
End point type	Secondary
End point timeframe: Baseline to week 104	

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[21]	
Units: percent				
arithmetic mean (standard deviation)	4.2 (± 8.3)	0 (± 0)	4.2 (± 8.3)	

Notes:

[21] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in radius trabecular separation
Statistical analysis description: Percent change in radius trabecular separation between baseline and week 104	
Comparison groups	Baseline pre-treatment v Teriparatide treatment
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	4.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	8.6
Variability estimate	Standard deviation
Dispersion value	8.3

Secondary: Percent change in tibia trabecular separation

End point title	Percent change in tibia trabecular separation
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End point description:

Percent change in tibia trabecular separation baseline to week 104

End point type	Secondary
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End point timeframe:

Baseline to week 104

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[22]	
Units: percent				
arithmetic mean (standard deviation)	1.9 (± 9.8)	0 (± 0)	1.9 (± 9.8)	

Notes:

[22] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in tibia trabecular separation
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Statistical analysis description:

Percent change in tibia trabecular separation between baseline and week 104

Comparison groups	Baseline pre-treatment v Teriparatide treatment
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Number of subjects included in analysis	32
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Analysis specification	Pre-specified
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Analysis type	other
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P-value	= 0.06
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Method	ANOVA
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Parameter estimate	Mean difference (final values)
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Point estimate	1.9
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Confidence interval

level	95 %
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sides	2-sided
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lower limit	-3.3
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upper limit	7.1
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Variability estimate	Standard deviation
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Dispersion value	9.8
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Secondary: Percent change in radius cortical volumetric bone mineral density (vBMD)

End point title	Percent change in radius cortical volumetric bone mineral density (vBMD)
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End point description:

Percent change in radius cortical volumetric bone mineral density (vBMD) between baseline and week 104

End point type	Secondary
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End point timeframe:

Baseline to week 104

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[23]	
Units: percent				
arithmetic mean (standard deviation)	-3.3 (± 5.8)	0 (± 0)	-3.3 (± 5.8)	

Notes:

[23] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in radius cortical vBMD
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Statistical analysis description:

Percent change in radius cortical vBMD between baseline and week 104

Comparison groups	Baseline pre-treatment v Teriparatide treatment
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.004
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.4
upper limit	-0.2
Variability estimate	Standard deviation
Dispersion value	5.8

Secondary: Percent change in tibia cortical volumetric bone mineral density (vBMD)

End point title	Percent change in tibia cortical volumetric bone mineral density (vBMD)
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End point description:

Percent change in tibia cortical vBMD between baseline and week 104

End point type	Secondary
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End point timeframe:

Baseline to week 104

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[24]	
Units: percent				
arithmetic mean (standard deviation)	-3.4 (± 3.7)	0 (± 0)	-3.4 (± 3.7)	

Notes:

[24] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in tibia cortical vBMD
Statistical analysis description:	
Percent change in tibia cortical vBMD between baseline and week 104	
Comparison groups	Baseline pre-treatment v Teriparatide treatment
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.4
upper limit	-1.4
Variability estimate	Standard deviation
Dispersion value	3.7

Secondary: Percent change in radius cortical thickness

End point title	Percent change in radius cortical thickness
End point description:	
Percent change in radius cortical thickness between baseline and week 104	
End point type	Secondary
End point timeframe:	
Baseline to week 104	

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[25]	
Units: percent				
arithmetic mean (standard deviation)	-4.7 (± 12.3)	0 (± 0)	-4.7 (± 12.3)	

Notes:

[25] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in radius cortical thickness
Statistical analysis description:	
Percent change in radius cortical thickness between baseline and week 104	
Comparison groups	Teriparatide treatment v Baseline pre-treatment
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.08
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-4.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.3
upper limit	1.9
Variability estimate	Standard error of the mean
Dispersion value	12.3

Secondary: Percent change in tibia cortical thickness

End point title	Percent change in tibia cortical thickness
End point description:	
Percent change in tibia cortical thickness between baseline and week 104	
End point type	Secondary
End point timeframe:	
Baseline to week 104	

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[26]	
Units: percent				
arithmetic mean (standard deviation)	-3.1 (± 8.9)	0 (± 0)	-3.1 (± 8.9)	

Notes:

[26] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in tibia cortical thickness
Statistical analysis description:	
Percent change in tibia cortical thickness between baseline and week 104	
Comparison groups	Baseline pre-treatment v Teriparatide treatment
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.002
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-3.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.8
upper limit	1.6
Variability estimate	Standard deviation
Dispersion value	8.9

Secondary: Percent change in radius cortical porosity

End point title	Percent change in radius cortical porosity
End point description:	
Percent change in radius cortical porosity between baseline and week 104	
End point type	Secondary
End point timeframe:	
Baseline to week 104	

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[27]	
Units: percent				
arithmetic mean (standard deviation)	21.2 (± 20.7)	0 (± 0)	21.2 (± 20.7)	

Notes:

[27] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in radius cortical porosity
Statistical analysis description: Percent change in radius cortical porosity between baseline and week 104	
Comparison groups	Baseline pre-treatment v Teriparatide treatment
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	21.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.2
upper limit	32.2
Variability estimate	Standard deviation
Dispersion value	20.7

Secondary: Percent change in tibia cortical porosity

End point title	Percent change in tibia cortical porosity
End point description: Percent change in tibia cortical porosity between baseline and week 104	
End point type	Secondary
End point timeframe: Baseline to week 104	

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[28]	
Units: percent				
arithmetic mean (standard deviation)	10.3 (± 17.5)	0 (± 0)	10.3 (± 17.5)	

Notes:

[28] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in tibia cortical porosity
Statistical analysis description: Percent change in tibia cortical porosity between baseline and week 104	
Comparison groups	Baseline pre-treatment v Teriparatide treatment

Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0002
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	10.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	19.6
Variability estimate	Standard deviation
Dispersion value	17.5

Secondary: Percent change radius cortical tissue mineral density (TMD)

End point title	Percent change radius cortical tissue mineral density (TMD)
End point description:	Percent change radius cortical tissue mineral density (TMD) between baseline and week 104
End point type	Secondary
End point timeframe:	Baseline to week 104

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[29]	
Units: percent				
arithmetic mean (standard deviation)	-3.2 (± 4.2)	0 (± 0)	-3.2 (± 4.2)	

Notes:

[29] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in radius cortical TMD
Statistical analysis description:	Percent change in radius cortical TMD between baseline and week 104
Comparison groups	Baseline pre-treatment v Teriparatide treatment
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.005
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-3.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.4
upper limit	-1
Variability estimate	Standard deviation
Dispersion value	4.2

Secondary: Percent change in tibia cortical tissue mineral density (TMD)

End point title	Percent change in tibia cortical tissue mineral density (TMD)
End point description: Percent change in tibia cortical tissue mineral density (TMD) between baseline and week 104	
End point type	Secondary
End point timeframe: Baseline to week 104	

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[30]	
Units: percent				
arithmetic mean (standard deviation)	-3.8 (± 3.6)	0 (± 0)	-3.8 (± 3.6)	

Notes:

[30] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in tibia cortical TMD
Statistical analysis description: Percent change in tibia cortical TMD between baseline and week 104	
Comparison groups	Baseline pre-treatment v Teriparatide treatment
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Median difference (final values)
Point estimate	-3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.7
upper limit	-1.9
Variability estimate	Standard deviation
Dispersion value	3.6

Secondary: Percent change in tibia stiffness

End point title	Percent change in tibia stiffness
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End point description:

Percent change in tibia stiffness between baseline and week 104

End point type	Secondary
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End point timeframe:

Baseline to week 104

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[31]	
Units: percent				
arithmetic mean (standard deviation)	-5.6 (± 23.1)	0 (± 0)	-5.6 (± 23.1)	

Notes:

[31] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in tibia stiffness
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Statistical analysis description:

Percent change in tibia stiffness between baseline and week 104

Comparison groups	Teriparatide treatment v Baseline pre-treatment
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Number of subjects included in analysis	32
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Analysis specification	Pre-specified
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Analysis type	other
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P-value	= 0.2
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Method	ANOVA
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Parameter estimate	Mean difference (final values)
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Point estimate	-5.6
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Confidence interval

level	95 %
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sides	2-sided
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lower limit	-17.9
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upper limit	6.7
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Variability estimate	Standard deviation
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Dispersion value	23.1
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Secondary: Percent change in radius failure load

End point title	Percent change in radius failure load
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End point description:

Percent change in radius failure load between baseline and week 104

End point type	Secondary
End point timeframe:	
Baseline to week 104	

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[32]	
Units: percent				
arithmetic mean (standard deviation)	0.6 (± 7.0)	0 (± 0)	0.6 (± 7.0)	

Notes:

[32] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in radius failure load
Statistical analysis description:	
Percent change in radius failure load between baseline and week 104	
Comparison groups	Teriparatide treatment v Baseline pre-treatment
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	4.3
Variability estimate	Standard deviation
Dispersion value	7

Secondary: Percent change in tibia failure load

End point title	Percent change in tibia failure load
End point description:	
Percent change in tibia failure load between baseline and week 104	
End point type	Secondary
End point timeframe:	
Baseline to week 104	

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[33]	
Units: percent				
arithmetic mean (standard deviation)	0.2 (± 4.4)	0 (± 0)	0.2 (± 4.4)	

Notes:

[33] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in tibia failure load
Statistical analysis description:	
Percent change in tibia failure load between baseline and week 104	
Comparison groups	Teriparatide treatment v Baseline pre-treatment
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.04
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	2.5
Variability estimate	Standard deviation
Dispersion value	4.4

Other pre-specified: Percent change in radius trabecular volumetric bone mineral density (vBMD)

End point title	Percent change in radius trabecular volumetric bone mineral density (vBMD)
End point description:	
Percent change in radius trabecular vBMD between baseline and week 104	
End point type	Other pre-specified
End point timeframe:	
Baseline to week 104	

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[34]	
Units: percent				
arithmetic mean (standard deviation)	-1.4 (± 6.3)	0 (± 0)	-1.4 (± 6.3)	

Notes:

[34] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in radius trabecular vBMD
Statistical analysis description:	
Percent change in radius trabecular vBMD between baseline and week 104	
Comparison groups	Teriparatide treatment v Baseline pre-treatment
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	2
Variability estimate	Standard deviation
Dispersion value	6.3

Post-hoc: Percent change in radius stiffness

End point title	Percent change in radius stiffness
End point description:	
Percent change in radius stiffness between baseline and week 104	
End point type	Post-hoc
End point timeframe:	
Baseline to week 104	

End point values	Teriparatide treatment	Baseline pre-treatment	Study completers	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16 ^[35]	
Units: percent				
arithmetic mean (standard deviation)	0.7 (± 8.1)	0 (± 0)	0.7 (± 8.1)	

Notes:

[35] - Per-protocol analysis for completers

Statistical analyses

Statistical analysis title	Percent change in radius stiffness
Statistical analysis description:	
Percent change in radius stiffness between baseline and week 104	
Comparison groups	Teriparatide treatment v Baseline pre-treatment
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.6
upper limit	5
Variability estimate	Standard deviation
Dispersion value	8.1

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Weeks: 0, 1, 2, 4, 12, 26, 39, 52, 65, 78, 91, 104

Adverse event reporting additional description:

Adverse event information including dates of event (including onset and resolution), event diagnosis and description, severity, assessment of relatedness to Forsteo or calcium/vitamin D supplements or vitamin D dosing and action taken was collected at visit 2 (baseline) and at each study visit thereafter.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.0
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Reporting groups

Reporting group title	Teriparatide (Forsteo) 20 mcg subcutaneous injection
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Reporting group description:

Teriparatide (Forsteo) 20 mcg subcutaneous injection once daily. Duration 104 weeks. This is a single arm study.

Serious adverse events	Teriparatide (Forsteo) 20 mcg subcutaneous injection		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 20 (15.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast lump			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Liver metastases			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Surgical and medical procedures			
Cystocele repair			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Teriparatide (Forsteo) 20 mcg subcutaneous injection		
Total subjects affected by non-serious adverse events subjects affected / exposed	19 / 20 (95.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Adrenal adenoma subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Haemangioma of liver subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Hepatic cyst subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Vascular disorders Blood pressure high subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2		
Hot flushes subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Sweating subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Surgical and medical procedures Dental fillings subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Dupuytren's contracture operation			

subjects affected / exposed occurrences (all) Mole excision subjects affected / exposed occurrences (all) Rodent ulcer excision subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		
General disorders and administration site conditions Inflammation at site of injection subjects affected / exposed occurrences (all) Injection site bruising subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		
Respiratory, thoracic and mediastinal disorders Chest infection subjects affected / exposed occurrences (all) Emphysema subjects affected / exposed occurrences (all) Shortness of breath subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 5 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		
Injury, poisoning and procedural complications Ankle injury subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Broken ankle subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		

Dislocated patella subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Cardiac disorders Generall unwell subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Palpitations subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 2		
Nervous system disorders Benign essential tremor subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Dizziness subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Fuzzy head subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Headache subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Pain in spine subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
TIA subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Eye disorders Conjunctivitis subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Gastrointestinal disorders Acid reflux (oesophageal) subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		

Constipation			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Diverticulitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Epidemic vomiting and diarrhoea			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	3		
Indigestion			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Stomach pain			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Stomach upset			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Itchy legs			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Rash both legs			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Rash on face			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Rash trunk			

subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Musculoskeletal and connective tissue disorders			
Bursitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Leg pain			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Plantar fasciitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Infections and infestations			
Common cold			
subjects affected / exposed	10 / 20 (50.00%)		
occurrences (all)	14		
Cough			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Dental abscess			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Head cold			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Leg infection			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Lethargy			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Sore throat			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Tonsillitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Viral sore throat			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
High cholesterol			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Hypercalcaemia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 January 2011	Substantial Amendment 01 [SA01] SA01 was submitted to the MHRA - to change the procedures required for testing, loading and retesting vitamin D levels. - reschedule a whole body DXA scan - add additional exclusion criteria to the sub-study protocol These changes were to ensure that only participants that meet the full eligibility criteria undertake research protocol procedures at visit 2. At the point of approval of this amendment, no participants had entered the study
16 October 2014	Substantial Amendment 05 [SA05] This amendment was to update the Reference Safety Information for the IMP Forsteo. An updated SmPC was submitted to the MHRA (SmPC Forsteo dated 25 April 2014). The Chief Investigator confirmed that the update RSI did not change the risk benefit assessment of the study, therefore no change to the protocol or other documents was made.

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.

This was an open-label study with no control group. Inclusion of a control group of postmenopausal women with osteoporosis was deemed to be unethical, and we assumed that the open-label design would not influence the study outcomes.

Notes: