Clinical trial results:
Teriparatide and Risedronate in the Treatment of Patients with Severe Postmenopausal Osteoporosis: Comparative Effects on vertebral Fractures

Summary

EudraCT number	2012-000123-41
Trial protocol	CZ BE ES DE AT IT HU GR PL
Global end of trial date	14 July 2016

Results information

Result version number	v1 (current)
This version publication date	30 July 2017
First version publication date	30 July 2017

Trial information

Trial identification

Sponsor protocol code	B3D-EW-GHDW

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01709110
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 14536, Trial Alias: B3D-EW-GHDW

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 July 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 July 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate if teriparatide 20 µg subcutaneously once daily is superior in reducing the incidence of new vertebral fractures during 24 months of therapy, when compared with risedronate 35 mg orally once weekly, in postmenopausal women with prevalent vertebral fragility fractures.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (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	23 October 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 118
Country: Number of subjects enrolled	Spain: 121
Country: Number of subjects enrolled	Austria: 53
Country: Number of subjects enrolled	Belgium: 87
Country: Number of subjects enrolled	Czech Republic: 136
Country: Number of subjects enrolled	France: 54
Country: Number of subjects enrolled	Germany: 68
Country: Number of subjects enrolled	Greece: 40
Country: Number of subjects enrolled	Hungary: 122
Country: Number of subjects enrolled	Italy: 69
Country: Number of subjects enrolled	Argentina: 157
Country: Number of subjects enrolled	United States: 122
Country: Number of subjects enrolled	Canada: 69
Country: Number of subjects enrolled	Brazil: 144
Worldwide total number of subjects	1360
EEA total number of subjects	868

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)	315
From 65 to 84 years	970
85 years and over	75

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, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Teriparatide

Arm description:

Teriparatide 20 microgram (µg) administered by subcutaneous (SC) injection once daily for 24 months.

Placebo given orally once weekly for 24 months.

All started participants received at least one dose of study drug; 683 participants were randomized.

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

Dosage and administration details:

Teriparatide 20 microgram (µg) administered by subcutaneous (SC) injection once daily for 24 months.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo given orally once weekly for 24 months.

Arm title	Risedronate

Arm description:

Risedronate 35 milligram (mg) administered orally once weekly for 24 months.

Placebo given by SC injection once daily for 24 months.

All started participants received at least one dose of study drug; 683 participants were randomized.

Arm type	Active comparator

Investigational medicinal product name	Risedronate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

isedronate 35 milligram (mg) administered orally once weekly for 24 months.

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:

Placebo given by SC injection once daily for 24 months.

Number of subjects in period 1	Teriparatide	Risedronate
Started	680	680
Completed	498	515
Not completed	182	165
Adverse event, serious fatal	14	6
Physician decision	4	10
Consent withdrawn by subject	94	87
Adverse event, non-fatal	56	48
Caregiver decision	1	1
Lost to follow-up	7	5
Sponsor decision	2	2
Lack of efficacy	1	1
Protocol deviation	3	5

Baseline characteristics

Reporting groups	
Reporting group title	Teriparatide

Reporting group description:

Teriparatide 20 microgram (µg) administered by subcutaneous (SC) injection once daily for 24 months.

Placebo given orally once weekly for 24 months.

All started participants received at least one dose of study drug; 683 participants were randomized.

Reporting group title	Risedronate

Reporting group description:

Risedronate 35 milligram (mg) administered orally once weekly for 24 months.

Placebo given by SC injection once daily for 24 months.

All started participants received at least one dose of study drug; 683 participants were randomized.

Reporting group values	Teriparatide	Risedronate	Total
Number of subjects	680	680	1360
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	72.6	71.6	
standard deviation	± 8.77	± 8.58	-
Gender categorical Units: Subjects			
Female	680	680	1360
Male	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	104	99	203
Not Hispanic or Latino	310	302	612
Unknown or Not Reported	266	279	545
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	1	2
Asian	4	8	12
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	5	15	20
White	670	653	1323
More than one race	0	3	3
Unknown or Not Reported	0	0	0
Distribution of Stratification Factors			
A participant was considered as having a recent clinical vertebral fragility fracture if she had at least one clinical vertebral fragility fracture within the last 12 months prior to baseline. A participant was considered a recent prior bisphosphonate user if she had received a total of 6 or more months of treatment with any oral bisphosphonate within 3 years prior to baseline.			
Units: Subjects			

Vertebral Fracture with Bisphosphonate Use	82	79	161
With Vertebral Fracture without Bisphosphonate Use	170	165	335
Without Vertebral Fracture with Bisphosphonate Use	184	189	373
Without Vertebral Fracture without Bisphosphonate	244	247	491
Vertebral Fracture Status			
According to Bioclinica spine x-ray central assessment at baseline.			
Units: Subjects			
<1 Fractures	0	0	0
1 Fracture	231	240	471
2 Fractures	178	174	352
3 Fractures	104	101	205
4 Fractures	60	62	122
5 or More Fractures	106	102	208
Not Applicable	1	1	2
Bone Mineral Density (BMD) Lumbar Spine			
Low BMD is defined as a lumbar spine, total hip or femoral neck BMD ≥ 1.5 standard deviation (SD) below the average BMD for young healthy, non-Hispanic, Caucasian women. Lumbar spine, total hip and femoral neck BMD were assessed by DXA by the investigator at baseline. Any lumbar vertebrae that were not analyzed due to artifacts, fracture, osteophytes, or other abnormalities, were excluded from the analysis; the number of participants analyzed for Teriparatide arm were 644 and Risedronate arm 653.			
Units: Gram per square centimeter (g/cm2)			
arithmetic mean	0.858	0.856	
standard deviation	± 0.1541	± 0.1473	-
Bone Mineral Density (BMD) Femoral Neck			
Low BMD is defined as a lumbar spine, total hip or femoral neck BMD ≥ 1.5 standard deviation (SD) below the average BMD for young healthy, non-Hispanic, Caucasian women. Lumbar spine, total hip and femoral neck BMD were assessed by DXA by the investigator at baseline. Any lumbar vertebrae that were not analyzed due to artifacts, fracture, osteophytes, or other abnormalities, were excluded from the analysis; the number of participants analyzed for Teriparatide arm were 658 and Risedronate arm 656.			
Units: g/cm2			
arithmetic mean	0.662	0.667	
standard deviation	± 0.1085	± 0.1129	-
Bone Mineral Density (BMD) Total Hip			
Low BMD is defined as a lumbar spine, total hip or femoral neck BMD ≥ 1.5 standard deviation (SD) below the average BMD for young healthy, non-Hispanic, Caucasian women. Lumbar spine, total hip and femoral neck BMD were assessed by DXA by the investigator at baseline. Any lumbar vertebrae that were not analyzed due to artifacts, fracture, osteophytes, or other abnormalities, were excluded from the analysis; the number of participants analyzed for Teriparatide arm were 633 and Risedronate arm 640.			
Units: g/cm2			
arithmetic mean	0.736	0.735	
standard deviation	± 0.1065	± 0.1165	-

End points

End points reporting groups

Reporting group title	Teriparatide

Reporting group description:

Teriparatide 20 microgram (µg) administered by subcutaneous (SC) injection once daily for 24 months.

Placebo given orally once weekly for 24 months.

All started participants received at least one dose of study drug; 683 participants were randomized.

Reporting group title	Risedronate

Reporting group description:

Risedronate 35 milligram (mg) administered orally once weekly for 24 months.

Placebo given by SC injection once daily for 24 months.

All started participants received at least one dose of study drug; 683 participants were randomized.

Primary: Proportion of Participants With New Vertebral Fractures

End point title	Proportion of Participants With New Vertebral Fractures

End point description:

The incidence of new vertebral fractures was assessed by quantitative vertebral morphometry measurements (QM) with qualitative visual semiquantitative grading (SQ) confirmation.

A new vertebral fracture was diagnosed in a vertebra that was non-fractured at the baseline radiological examination. It was defined as a loss of vertebral body height of at least 20% and 4 mm from the baseline radiograph by vertebral QM, based upon placement of six points by a trained, central reader. Any fractures identified by QM were confirmed using SQ: if the vertebral body also had an increase of one or more severity grade, it was considered an incident vertebral fracture.

Analysis Population Description: Full analysis set-modified: participants with baseline and at least one post-baseline spinal radiograph evaluable to assess the vertebral fracture status after 24 month of therapy.

End point type	Primary

End point timeframe:

Baseline through 24 Months

End point values	Teriparatide	Risedronate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	516	533		
Units: Participants (with at least one event)				
number (not applicable)	28	64		

Statistical analyses

Statistical analysis title	Primary Endpoint Odds Ratio
Comparison groups	Risedronate v Teriparatide

Number of subjects included in analysis	1049
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.000094 [1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.4071
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.256
upper limit	0.647

Notes:

[1] - Cochran-Mantel-Haenszel test was adjusted for the antecedent of recent clinical vertebral fractures and recent bisphosphonate use.

Statistical analysis title	Primary Endpoint Risk Ratio
Comparison groups	Teriparatide v Risedronate
Number of subjects included in analysis	1049
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.000094 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	0.4431
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	0.677

Notes:

[2] - Cochran-Mantel-Haenszel test was adjusted for the antecedent of recent clinical vertebral fractures and recent bisphosphonate use.

Secondary: Proportion of Participants With Pooled New and Worsening Vertebral Fractures

End point title	Proportion of Participants With Pooled New and Worsening Vertebral Fractures

End point description:

Worsening of a pre-existing fracture was considered if the decrease in vertebral height was at least one severity grade in the semi-quantitative assessment, confirmed by a trained central reader, where vertebrae were graded as normal (SQ0) or as with mild (SQ1), moderate (SQ2), or severe (SQ3) fractures, defined as ~20 to 25% (mild), ~25 to 40% (moderate) or ~40% or more (severe) decrease in anterior, central, or posterior vertebral height (T4 to L4).

Analysis Population Description: Full analysis set-modified: participants with baseline and at least one post-baseline spinal radiograph evaluable to assess the vertebral fracture status after 24 month of therapy.

End point type	Secondary

End point timeframe:

Baseline through 24 Months

End point values	Teriparatide	Risedronate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	516	533		
Units: Participants (with at least one event)				
number (not applicable)	31	69		

Statistical analyses

Statistical analysis title	Risk Ratio
Comparison groups	Teriparatide v Risedronate
Number of subjects included in analysis	1049
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.000075 [3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	0.4561
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.305
upper limit	0.682

Notes:

[3] - Cochran-Mantel-Haenszel was adjusted for the antecedent of recent clinical vertebral fractures and recent bisphosphonate use.

Statistical analysis title	Odds Ratio
Comparison groups	Teriparatide v Risedronate
Number of subjects included in analysis	1049
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.000075 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.4187
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.269
upper limit	0.652

Notes:

[4] - Cochran-Mantel-Haenszel was adjusted for the antecedent of recent clinical vertebral fractures and recent bisphosphonate use.

Secondary: Proportion of Participants With Pooled Clinical Vertebral and Non-Vertebral Fragility Fractures

End point title	Proportion of Participants With Pooled Clinical Vertebral and Non-Vertebral Fragility Fractures

End point description:

A clinical vertebral fracture was defined as a new or worsening vertebral fracture, confirmed by radiography, that was associated with signs and symptoms highly suggestive of a vertebral fracture.

All non-vertebral fractures that occurred and were diagnosed between visits required the confirmation by the site investigators after evaluating the original x-ray film(s), the radiology or surgical report. For clinical vertebral fractures, the final confirmation of the diagnosis required the centralized evaluation by a trained, independent reader.

Analysis Population Description: Full analysis set: all participants who received at least one dose of study drug and had evaluable data.

End point type	Secondary

End point timeframe:

Baseline through 24 Months

End point values	Teriparatide	Risedronate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	680	680		
Units: Participants (with at least one event)				
number (not applicable)	30	61		

Statistical analyses

Statistical analysis title	Stratified Hazard Ratio
Comparison groups	Teriparatide v Risedronate
Number of subjects included in analysis	1360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.000869 [5]
Method	Stratified Log Rank
Parameter estimate	Stratified Hazard Ratio (HR)
Point estimate	0.4831
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.316
upper limit	0.739

Notes:

[5] - Stratified Log Rank test was adjusted for the antecedent of recent clinical vertebral fractures and recent bisphosphonate use.

Secondary: Proportion of Participants With Non-Vertebral Fragility Fractures

End point title	Proportion of Participants With Non-Vertebral Fragility Fractures

End point description:

A non-vertebral fracture is a fracture at any of the following non-vertebral sites: clavicle, scapula, ribs, sternum, sacrum, coccyx, humerus, radius, ulna, carpus, pelvis, hip, femur, patella, tibia, fibula, ankle, calcaneus, tarsus, and metatarsal. Non-vertebral fractures were determined by direct questioning at each visit, and confirmed by the site investigators by x-ray, radiology or surgical report. Fractures resulting from a severe trauma such as a traffic collision, a beating, or having been struck by a falling or moving object were not considered fragility fractures but traumatic fractures.

Analysis Population Description: Full analysis set: all participants who received at least one dose of study drug and had evaluable data.

End point type	Secondary

End point timeframe:

Baseline through 24 Months

End point values	Teriparatide	Risedronate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	680	680		
Units: Participants (with at least one event)				
number (not applicable)	25	38		

Statistical analyses

Statistical analysis title	Stratified Hazard Ratio (HR)
Comparison groups	Teriparatide v Risedronate
Number of subjects included in analysis	1360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.099023 [6]
Method	Stratified Log Rank
Parameter estimate	Stratified Hazard Ratio (HR)
Point estimate	0.6553
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	1.101

Notes:

[6] - Stratified Log Rank test was adjusted for the antecedent of recent clinical vertebral fractures and recent bisphosphonate use.

Secondary: Proportion of Participants With Major Non-Vertebral Fragility Fractures

End point title	Proportion of Participants With Major Non-Vertebral Fragility Fractures

End point description:

A major non-vertebral fracture is a fracture at any of the following non-vertebral sites hip, radius, humerus, ribs, pelvis, tibia and femur. Non-vertebral fractures were determined by direct questioning at each visit, and confirmed by the site investigators by x-ray, radiology or surgical report. Fractures resulting from a severe trauma such as a traffic collision, a beating, or having been struck by a falling or moving.

Analysis Population Description: Full analysis set: all participants who received at least one dose of study drug and had evaluable data.

End point type	Secondary

End point timeframe:

Baseline through 24 Months

End point values	Teriparatide	Risedronate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	680	680		
Units: Participants (with at least one event				
number (not applicable)	18	31		

Statistical analyses

Statistical analysis title	Stratified Hazard Ratio
Comparison groups	Teriparatide v Risedronate
Number of subjects included in analysis	1360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.062432 [7]
Method	Stratified Log Rank
Parameter estimate	Stratified Hazard Ratio (HR)
Point estimate	0.5786
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.318
upper limit	1.052

Notes:

[7] - Stratified Log Rank test was adjusted for the antecedent of recent clinical vertebral fractures and recent bisphosphonate use.

Secondary: Proportion of Participants With New Moderate and/or Severe Vertebral Fractures

End point title	Proportion of Participants With New Moderate and/or Severe Vertebral Fractures

End point description:

Vertebrae were graded as moderate (SQ2), or severe (SQ3) fractures, based on ~25 to 40% (moderate) or ~40% or more (severe) decrease in anterior, central, or posterior vertebral height (T4 through L4).

Analysis Population Description: Full analysis set-modified: participants with baseline and at least one post-baseline spinal radiograph evaluable to assess the vertebral fracture status after 24 month of therapy.

End point type	Secondary

End point timeframe:

Baseline through 24 Months

End point values	Teriparatide	Risedronate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	516	533		
Units: Participants (with at least one event)				
number (not applicable)	26	63		

Statistical analyses

Statistical analysis title	Odds Ratio
Comparison groups	Teriparatide v Risedronate
Number of subjects included in analysis	1049
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [8]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.3812
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.237
upper limit	0.614

Notes:

[8] - 0.001

Statistical analysis title	Risk Ratio
Comparison groups	Teriparatide v Risedronate
Number of subjects included in analysis	1049
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [9]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	0.4173
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.27
upper limit	0.646

Notes:

[9] - Cochran-Mantel-Haenszel test was adjusted for the antecedent of recent clinical vertebral fractures and recent bisphosphonate use.

Secondary: Proportion of Participants With New Multiple (2 or More) Vertebral Fractures

End point title	Proportion of Participants With New Multiple (2 or More) Vertebral Fractures

End point description:

Analysis Population Description: Full analysis set-modified: participants with baseline and at least one post-baseline spinal radiograph evaluable to assess the vertebral fracture status after 24 month of therapy.

End point type	Secondary

End point timeframe:

Baseline through 24 Months

End point values	Teriparatide	Risedronate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	516	533		
Units: Participants (with at least one event)				
number (not applicable)	2	12		

Statistical analyses

Statistical analysis title	Odds Ratio
Comparison groups	Teriparatide v Risedronate
Number of subjects included in analysis	1049
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007 [10]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.1593
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.035
upper limit	0.728

Notes:

[10] - Cochran-Mantel-Haenszel test was adjusted for the antecedent of recent clinical vertebral fractures and recent bisphosphonate use.

Statistical analysis title	Risk Ratio
Comparison groups	Teriparatide v Risedronate
Number of subjects included in analysis	1049
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007 [11]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	0.1643

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.036
upper limit	0.744

Notes:

[11] - Cochran-Mantel-Haenszel test was adjusted for the antecedent of recent clinical vertebral fractures and recent bisphosphonate use.

Secondary: Proportion of Participants With Pooled Fragility and Traumatic Non-Vertebral Fractures

End point title	Proportion of Participants With Pooled Fragility and Traumatic Non-Vertebral Fractures

End point description:

Traumatic fractures were considered if resulting from a severe trauma such as a traffic collision, a beating, or having been struck by a falling or moving object.

Analysis Population Description: Full analysis set: all participants who received at least one dose of study drug and had evaluable data.

End point type	Secondary

End point timeframe:

Baseline through 24 Months

End point values	Teriparatide	Risedronate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	680	680		
Units: Participants (with at least one event)				
number (not applicable)	40	57		

Statistical analyses

Statistical analysis title	Stratified Hazard Ratio
Comparison groups	Teriparatide v Risedronate
Number of subjects included in analysis	1360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.078 [12]
Method	Stratified Log Rank
Parameter estimate	Stratified Hazard Ratio (HR)
Point estimate	0.696
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.461
upper limit	1.05

Notes:

[12] - Stratified Log Rank test was adjusted for the antecedent of recent clinical vertebral fractures and recent bisphosphonate use.

Secondary: Change From Baseline to 24 Months Endpoint in Height

End point title	Change From Baseline to 24 Months Endpoint in Height

End point description:

Analysis Population Description: Full analysis set: all participants who received at least one dose of study drug and had evaluable data.

End point type	Secondary

End point timeframe:

Baseline, 24 Months

End point values	Teriparatide	Risedronate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	565	580		
Units: Centimeter (cm)				
arithmetic mean (standard deviation)				
Baseline	154.7 (± 7.15)	155 (± 7.4)		
24 Months	154.3 (± 7.05)	154.5 (± 7.42)		

Statistical analyses

Statistical analysis title	Least Square Means
Comparison groups	Teriparatide v Risedronate
Number of subjects included in analysis	1145
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.093 [13]
Method	Mixed models analysis
Parameter estimate	Least Square Means
Point estimate	-0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.28
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	0.08

Notes:

[13] - Model included the following fixed effects: treatment, visit, treatment-by-visit interaction, antecedent of recent clinical vertebral fractures, recent use of bisphosphonate and baseline body height (cm).

Secondary: Change From Baseline to 24 Months Endpoint in Back Pain Using an 11-point Numerical Pain Rating Scale

End point title	Change From Baseline to 24 Months Endpoint in Back Pain Using an 11-point Numerical Pain Rating Scale

End point description:

Participants rated the worst back pain during the 24 hours preceding the visit at baseline and each post-baseline visit. An 11-point numerical back pain rating scale (rated from 0 = no back pain to 10 = worst possible back pain) was used.

Analysis Population Description: Full analysis set: all participants who received at least one dose of study drug and had evaluable data.

End point type	Secondary

End point timeframe:

Baseline, 24 Months

End point values	Teriparatide	Risedronate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	642	648		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	4.5 (± 2.9)	4.5 (± 2.91)		
24 Months	3.4 (± 2.95)	3.4 (± 2.89)		

Statistical analyses

Statistical analysis title	Least Square Means
Comparison groups	Teriparatide v Risedronate
Number of subjects included in analysis	1290
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.585 [14]
Method	Mixed models analysis
Parameter estimate	Least Square Means
Point estimate	-0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.42
upper limit	0.24
Variability estimate	Standard error of the mean
Dispersion value	0.17

Notes:

[14] - Model included the following fixed effects: treatment, visit, treatment-by-visit interaction, antecedent of recent clinical vertebral fractures, recent use of bisphosphonate and baseline back pain (no pain - worst pain [0-10]).

Secondary: Change From Baseline to 24 Months Endpoint in the European Quality of Life Questionnaire [EQ-5D-5L] (UK)

End point title	Change From Baseline to 24 Months Endpoint in the European Quality of Life Questionnaire [EQ-5D-5L] (UK)

End point description:

The EQ-5D is a generic, multidimensional, health-related, quality-of-life instrument and was completed on five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) to

measure health-related quality of life on a scale from 0-1, with the higher score indicating a better health state perceived by the participant. The profile allowed participants to rate their health state in 5 health domains: mobility, self-care, usual activities, pain/discomfort, and mood using a three level scale (no problem, some problems, and major problems). These combinations of attributes were converted into a weighted health-state Index Score according to the UK population-based algorithm.

Analysis Population Description: Full analysis set: all participants who received at least one dose of study drug and had evaluable data.

End point type	Secondary

End point timeframe:

Baseline, 24 Months

End point values	Teriparatide	Risedronate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	642	647		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	0.59 (± 0.243)	0.62 (± 0.228)		
24 Months	0.65 (± 0.249)	0.68 (± 0.205)		

Statistical analyses

Statistical analysis title	Least Square Means
Comparison groups	Teriparatide v Risedronate
Number of subjects included in analysis	1289
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.757 [15]
Method	Mixed models analysis
Parameter estimate	Least Square Means
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	0.01

Notes:

[15] - Model included the following fixed effects: treatment, visit, treatment-by-visit interaction, antecedent of recent clinical vertebral fractures, recent use of bisphosphonate baseline EQ-5D-5L (UK).

Secondary: Change From Baseline to 24 Months Endpoint in the European Quality of Life Questionnaire [EQ-5D-5L] (US)

End point title	Change From Baseline to 24 Months Endpoint in the European Quality of Life Questionnaire [EQ-5D-5L] (US)

End point description:

The same EQ-5D-5L results were converted into a weighted health-state Index Score according to the USA population-based algorithm.

Analysis Population Description: Full analysis set: all participants who received at least one dose of study drug and had evaluable data.

End point type	Secondary

End point timeframe:

Baseline, 24 Months

End point values	Teriparatide	Risedronate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	642	647		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	0.7 (± 0.167)	0.72 (± 0.159)		
24 Months	0.74 (± 0.176)	0.76 (± 0.145)		

Statistical analyses

Statistical analysis title	Least Square Means
Comparison groups	Teriparatide v Risedronate
Number of subjects included in analysis	1289
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.694 [16]
Method	Mixed models analysis
Parameter estimate	Least Square Means
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02
upper limit	0.01
Variability estimate	Standard error of the mean
Dispersion value	0.01

Notes:

[16] - Model included the following fixed effects: treatment, visit, treatment-by-visit interaction, antecedent of recent clinical vertebral fractures, recent use of bisphosphonate baseline EQ-5D-5L (US).

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All randomized participants

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Teriparatide

Reporting group description:

Teriparatide 20 microgram administered by subcutaneous injection once daily for 24 months.

Placebo given orally once weekly for 24 months.

Reporting group title	Risedronate

Reporting group description:

Risedronate 35 milligram administered orally once weekly for 24 months.

Placebo given by SC injection once daily for 24 months.

Serious adverse events	Teriparatide	Risedronate	
Total subjects affected by serious adverse events			
subjects affected / exposed	138 / 683 (20.20%)	117 / 683 (17.13%)	
number of deaths (all causes)	15	7	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	1 / 683 (0.15%)	2 / 683 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			

subjects affected / exposed	3 / 683 (0.44%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer metastatic			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast neoplasm			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervix carcinoma			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chondrosarcoma			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystadenocarcinoma ovary			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial cancer			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypergammaglobulinaemia benign monoclonal			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive breast carcinoma			

subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 683 (0.15%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal cancer			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Metastases to bone			
subjects affected / exposed	2 / 683 (0.29%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-small cell lung cancer			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cancer			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma metastatic			

subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papillary thyroid cancer			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma cell myeloma			
subjects affected / exposed	1 / 683 (0.15%)	2 / 683 (0.29%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	1 / 1	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic stenosis			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial disorder			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			

subjects affected / exposed	2 / 683 (0.29%)	3 / 683 (0.44%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Granulomatosis with polyangiitis			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	1 / 683 (0.15%)	2 / 683 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	0 / 683 (0.00%)	2 / 683 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemic shock			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	4 / 683 (0.59%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subclavian artery occlusion			

subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vena cava thrombosis			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Oedema peripheral			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Performance status decreased			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Sudden cardiac death			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Reproductive system and breast disorders			
Female genital tract fistula			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ovarian cyst			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine prolapse			
subjects affected / exposed	1 / 683 (0.15%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	1 / 683 (0.15%)	2 / 683 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	1 / 683 (0.15%)	2 / 683 (0.29%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
Chronic obstructive pulmonary disease			
subjects affected / exposed	2 / 683 (0.29%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Chronic respiratory failure			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemothorax			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Laryngospasm			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			
subjects affected / exposed	1 / 683 (0.15%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	3 / 683 (0.44%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	2 / 683 (0.29%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			

subjects affected / exposed	1 / 683 (0.15%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major depression			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device dislocation			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device malfunction			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood pressure increased			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carbohydrate antigen 19-9 increased			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical condition abnormal			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural			

complications				
Ankle fracture				
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Cervical vertebral fracture				
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Clavicle fracture				
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Concussion				
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Contusion				
subjects affected / exposed	0 / 683 (0.00%)	2 / 683 (0.29%)		
occurrences causally related to treatment / all	0 / 0	0 / 2		
deaths causally related to treatment / all	0 / 0	0 / 0		
Craniocerebral injury				
subjects affected / exposed	2 / 683 (0.29%)	1 / 683 (0.15%)		
occurrences causally related to treatment / all	1 / 2	0 / 1		
deaths causally related to treatment / all	1 / 1	0 / 0		
Fall				
subjects affected / exposed	15 / 683 (2.20%)	19 / 683 (2.78%)		
occurrences causally related to treatment / all	1 / 16	0 / 21		
deaths causally related to treatment / all	1 / 1	0 / 0		
Femoral neck fracture				
subjects affected / exposed	4 / 683 (0.59%)	3 / 683 (0.44%)		
occurrences causally related to treatment / all	0 / 4	0 / 3		
deaths causally related to treatment / all	0 / 0	0 / 0		
Femur fracture				

subjects affected / exposed	3 / 683 (0.44%)	6 / 683 (0.88%)	
occurrences causally related to treatment / all	0 / 4	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	0 / 683 (0.00%)	2 / 683 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	1 / 683 (0.15%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	1 / 1	1 / 1	
Forearm fracture			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	1 / 683 (0.15%)	5 / 683 (0.73%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	3 / 683 (0.44%)	5 / 683 (0.73%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional hernia			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury			

subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	3 / 683 (0.44%)	6 / 683 (0.88%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Overdose			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patella fracture			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	0 / 683 (0.00%)	3 / 683 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural stroke			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural nausea			

subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural vomiting			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	2 / 683 (0.29%)	2 / 683 (0.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	3 / 683 (0.44%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scapula fracture			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	0 / 683 (0.00%)	2 / 683 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous haematoma			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			

subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	2 / 683 (0.29%)	3 / 683 (0.44%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulna fracture			
subjects affected / exposed	1 / 683 (0.15%)	3 / 683 (0.44%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	1 / 683 (0.15%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Left ventricle outflow tract obstruction			

subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	3 / 683 (0.44%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Angina pectoris			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	5 / 683 (0.73%)	3 / 683 (0.44%)	
occurrences causally related to treatment / all	0 / 5	1 / 3	
deaths causally related to treatment / all	0 / 0	1 / 1	
Atrioventricular block			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	0 / 683 (0.00%)	2 / 683 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Cardiac failure			
subjects affected / exposed	2 / 683 (0.29%)	2 / 683 (0.29%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
Cardiac failure congestive			

subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac valve disease			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	1 / 683 (0.15%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	2 / 683 (0.29%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	1 / 1	1 / 1	
Pericarditis			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tricuspid valve incompetence			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Carotid artery stenosis			

subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar ischaemia			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral artery embolism			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	2 / 683 (0.29%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	2 / 2	0 / 0	
Depressed level of consciousness			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolic stroke			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intercostal neuralgia			

subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	2 / 683 (0.29%)	3 / 683 (0.44%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple sclerosis			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radicular pain			
subjects affected / exposed	1 / 683 (0.15%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiculopathy			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	2 / 683 (0.29%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord compression			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			

subjects affected / exposed	3 / 683 (0.44%)	2 / 683 (0.29%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	2 / 683 (0.29%)	2 / 683 (0.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tremor			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular dementia			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular encephalopathy			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Coagulopathy			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemolytic anaemia			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune thrombocytopenic purpura			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microcytic anaemia			

subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pernicious anaemia			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	2 / 683 (0.29%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 683 (0.00%)	3 / 683 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenitis			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			

subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	2 / 683 (0.29%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral hernia, obstructive			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis erosive			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 683 (0.15%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			

subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal achalasia			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic cyst			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 683 (0.15%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Regurgitation			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			

subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	0 / 683 (0.00%)	2 / 683 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic hepatitis			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic lupus erythematosus rash			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 683 (0.29%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus urinary			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hydronephrosis			
subjects affected / exposed	0 / 683 (0.00%)	2 / 683 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrotic syndrome			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Renal impairment			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 683 (0.44%)	5 / 683 (0.73%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kyphosis			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Lumbar spinal stenosis			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteitis			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	3 / 683 (0.44%)	4 / 683 (0.59%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periostitis			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudarthrosis			
subjects affected / exposed	1 / 683 (0.15%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid arthritis			
subjects affected / exposed	1 / 683 (0.15%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	2 / 683 (0.29%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column stenosis			

subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovial cyst			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon disorder			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebral foraminal stenosis			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal sepsis			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	3 / 683 (0.44%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			

subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia pyelonephritis			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	2 / 683 (0.29%)	3 / 683 (0.44%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	3 / 683 (0.44%)	3 / 683 (0.44%)	
occurrences causally related to treatment / all	1 / 3	1 / 3	
deaths causally related to treatment / all	1 / 1	1 / 1	
Postoperative wound infection			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyonephrosis			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 683 (0.15%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Urinary tract infection			
subjects affected / exposed	2 / 683 (0.29%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperlipidaemia			

subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	1 / 683 (0.15%)	0 / 683 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 683 (0.00%)	1 / 683 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 683 (0.00%)	2 / 683 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Teriparatide	Risedronate	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	130 / 683 (19.03%)	130 / 683 (19.03%)	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	44 / 683 (6.44%)	51 / 683 (7.47%)	
occurrences (all)	54	63	
Back pain			
subjects affected / exposed	73 / 683 (10.69%)	79 / 683 (11.57%)	
occurrences (all)	77	89	
Pain in extremit			
subjects affected / exposed	37 / 683 (5.42%)	0 / 683 (0.00%)	
occurrences (all)	45	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported