Clinical trial results:
A Multicenter, Randomized, Multiple-dose Phase 3 Study to Evaluate the Noninferiority of Romosozumab at a 90 mg/mL Concentration Compared With a 70 mg/mL Concentration in Postmenopausal Women With Osteoporosis

Summary

EudraCT number	2013-000434-35
Trial protocol	PL CZ
Global end of trial date	08 December 2014

Results information

Result version number	v1 (current)
This version publication date	17 July 2016
First version publication date	17 July 2016

Trial information

Trial identification

Sponsor protocol code	20120156

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02016716
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen, Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States, 91320
Public contact	IHQ-Medical Info - Clinical Trials, Amgen (Europe) GmbH, MedinfoInternational@amgen.com
Scientific contact	IHQ-Medical Info - Clinical Trials, Amgen (Europe) GmbH, MedinfoInternational@amgen.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	08 December 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 December 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the non-inferiority of a 6-month treatment with 210 mg romosozumab administered every month (QM) using a 90 mg/mL concentration compared with 210 mg romosozumab QM using a 70 mg/mL concentration on percent change from baseline in bone mineral density (BMD) at the lumbar spine as assessed by dual-energy x-ray absorptiometry (DXA) in postmenopausal women with osteoporosis.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) and applicable country regulations/guidelines.
The protocol, informed consent form (ICF), other written subject information were submitted to the applicable Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for written approval , which was received by Amgen before recruitment of subjects into the study and shipment of Amgen investigational product.
All subjects provided written informed consent after the aims, methods, and potential risks of the study were adequately explained. Informed consent was obtained before any protocol-specific screening procedures or any investigational products were administered.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 December 2013
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: 250
Country: Number of subjects enrolled	Czech Republic: 15
Country: Number of subjects enrolled	United States: 29
Worldwide total number of subjects	294
EEA total number of subjects	265

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)	115
From 65 to 84 years	175
85 years and over	4

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 11 centers: 7 in Poland, 2 in the Czech Republic, and 2 in the United States. The First subject enrolled on 03 December 2013 and the last subject enrolled on 07 March 2014.

Pre-assignment

Screening details:

After signing informed consent subjects entered a screening period to complete eligibility assessments. Eligible subjects were randomized in a 22:5:22:5 ratio to
•romosozumab 90 mg/mL
•placebo 90 mg/mL
•romosozumab 70 mg/mL
•placebo 70 mg/mL
For efficacy analyses the 2 placebo groups were combined, for safety the data are reported separately.

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

Blinding implementation details:

Randomization was double-blind within the concentrations (romosozumab 90 mg/mL and placebo 90 mg/mL; romosozumab 70 mg/mL and placebo 70 mg/mL).

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received matching placebo (either administered as 2 subcutaneous (SC) injections of 1.17 mL or 3 SC injections of 1.0 mL) every month for 6 months.

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

Dosage and administration details:

Administered by subcutaneous injection once a month

Arm title	Romosozumab 70 mg/mL

Arm description:

Participants received 210 mg romosozumab monthly, administered as 3 subcutaneous 1 mL injections of a 70 mg/mL solution, for 6 months.

Arm type	Experimental
Investigational medicinal product name	Romosozumab
Investigational medicinal product code	AMG 785
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered as 3 SC injections of a 70 mg/mL concentration in a 1.0 mL glass prefilled syringe.

Arm title	Romosozumab 90 mg/mL

Arm description:

Participants received 210 mg romosozumab monthly, administered as 2 subcutaneous 1.17 mL injections of a 90 mg/mL solution, for 6 months.

Arm type	Experimental
Investigational medicinal product name	Romosozumab
Investigational medicinal product code	AMG 785
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered as 2 SC injections of a 90 mg/mL concentration in a 1.17 mL crystal zenith resin prefilled syringe.

Number of subjects in period 1	Placebo	Romosozumab 70 mg/mL	Romosozumab 90 mg/mL
Started	53	118	123
Completed	47	110	117
Not completed	6	8	6
Consent withdrawn by subject	5	5	5
Lost to follow-up	1	2	1
Protocol-specified criteria	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received matching placebo (either administered as 2 subcutaneous (SC) injections of 1.17 mL or 3 SC injections of 1.0 mL) every month for 6 months.	
Reporting group title	Romosozumab 70 mg/mL
Reporting group description:	
Participants received 210 mg romosozumab monthly, administered as 3 subcutaneous 1 mL injections of a 70 mg/mL solution, for 6 months.	
Reporting group title	Romosozumab 90 mg/mL
Reporting group description:	
Participants received 210 mg romosozumab monthly, administered as 2 subcutaneous 1.17 mL injections of a 90 mg/mL solution, for 6 months.	

Reporting group values	Placebo	Romosozumab 70 mg/mL	Romosozumab 90 mg/mL
Number of subjects	53	118	123
Age categorical Units: Subjects			
< 65 years	23	46	46
≥ 65 years	30	72	77
Age continuous Units: years			
arithmetic mean	68.4	67.4	67.7
standard deviation	± 8	± 7.1	± 7.6
Gender categorical Units: Subjects			
Female	53	118	123
Male	0	0	0
Race Units: Subjects			
Asian	0	2	0
Black (or African American)	0	1	0
White	53	115	123
Lumbar Spine Bone Mineral Density (BMD) T-score			
The T-score is the bone mineral density (BMD) at the site when compared to that of a healthy thirty-year-old. Normal is a T-score of −1.0 or higher; Osteopenia is defined as between −1.0 and −2.5; Osteoporosis is defined as −2.5 or lower, meaning a bone density that is two and a half standard deviations below the mean of a thirty-year-old man/woman.			
Units: T-score			
arithmetic mean	-2.842	-2.965	-3.029
standard deviation	± 1.033	± 0.96	± 0.687
Total Hip BMD T-score Units: T-score			
arithmetic mean	-2.057	-1.819	-1.828
standard deviation	± 0.634	± 0.673	± 0.649
Femoral Neck BMD T-score Units: T-score			
arithmetic mean	-2.304	-2.139	-2.018

standard deviation	± 0.517	± 0.611	± 0.593
Serum Procollagen Type 1 N-telopeptide (P1NP)			
Units: µg/L			
median	49	53	50
inter-quartile range (Q1-Q3)	38 to 61	40 to 61	40 to 64
Serum Type 1 Collagen C-telopeptide (CTX)			
Units: ng/L			
median	426.5	440	402
inter-quartile range (Q1-Q3)	296.5 to 560.5	288 to 613	299 to 530

Reporting group values	Total		
Number of subjects	294		
Age categorical			
Units: Subjects			
< 65 years	115		
≥ 65 years	179		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	294		
Male	0		
Race			
Units: Subjects			
Asian	2		
Black (or African American)	1		
White	291		
Lumbar Spine Bone Mineral Density (BMD) T-score			
The T-score is the bone mineral density (BMD) at the site when compared to that of a healthy thirty-year-old. Normal is a T-score of −1.0 or higher; Osteopenia is defined as between −1.0 and −2.5; Osteoporosis is defined as −2.5 or lower, meaning a bone density that is two and a half standard deviations below the mean of a thirty-year-old man/woman.			
Units: T-score			
arithmetic mean			
standard deviation	-		
Total Hip BMD T-score			
Units: T-score			
arithmetic mean			
standard deviation	-		
Femoral Neck BMD T-score			
Units: T-score			
arithmetic mean			
standard deviation	-		
Serum Procollagen Type 1 N-telopeptide (P1NP)			
Units: µg/L			
median			
inter-quartile range (Q1-Q3)	-		
Serum Type 1 Collagen C-telopeptide			

(CTX) Units: ng/L median inter-quartile range (Q1-Q3)	- -		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received matching placebo (either administered as 2 subcutaneous (SC) injections of 1.17 mL or 3 SC injections of 1.0 mL) every month for 6 months.	
Reporting group title	Romosozumab 70 mg/mL
Reporting group description:	
Participants received 210 mg romosozumab monthly, administered as 3 subcutaneous 1 mL injections of a 70 mg/mL solution, for 6 months.	
Reporting group title	Romosozumab 90 mg/mL
Reporting group description:	
Participants received 210 mg romosozumab monthly, administered as 2 subcutaneous 1.17 mL injections of a 90 mg/mL solution, for 6 months.	

Primary: Percent Change From Baseline in Bone Mineral Density (BMD) at the Lumbar Spine

End point title	Percent Change From Baseline in Bone Mineral Density (BMD) at the Lumbar Spine
End point description:	
Bone mineral density was measured by dual-energy X-ray absorptiometry (DXA).	
End point type	Primary
End point timeframe:	
Baseline and month 6	

End point values	Placebo	Romosozumab 70 mg/mL	Romosozumab 90 mg/mL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	46[1]	110[2]	117[3]	
Units: percent change				
least squares mean (confidence interval 95%)	0.8 (-0.4 to 2.1)	9.6 (8.8 to 10.4)	9.2 (8.4 to 10)	

Notes:

[1] - Subjects with values at baseline and at month 6

[2] - Subjects with values at baseline and at month 6

[3] - Subjects with values at baseline and at month 6

Statistical analyses

Statistical analysis title	Non-inferiority Analysis
Statistical analysis description:	
For the evaluation of the non-inferiority hypothesis, the least squares mean of the treatment difference for romosozumab treatment groups only (romosozumab 90 mg/mL - romosozumab 70 mg/mL) and the corresponding lower 1-sided 97.5% CI was estimated using an ANCOVA model adjusting for treatment, and baseline lumbar spine BMD T-score.	
Comparison groups	Romosozumab 70 mg/mL v Romosozumab 90 mg/mL

Number of subjects included in analysis	227
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	Least Squares Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	0.7

Notes:

[4] - The primary hypothesis was that the mean percent change from baseline in lumbar spine BMD at month 6 in subjects receiving romosozumab 210 mg QM using the 90 mg/mL concentration would not be inferior to that in subjects receiving romosozumab 210 mg QM using the 70 mg/mL concentration using a margin of -2.0%.

Secondary: Percent Change From Baseline in Total Hip BMD

End point title	Percent Change From Baseline in Total Hip BMD

End point description:

Total hip BMD was measured using DXA. Analysis was based on ANCOVA model adjusting for treatment, and baseline total hip BMD T score.

End point type	Secondary

End point timeframe:

Baseline and month 6

End point values	Placebo	Romosozumab 70 mg/mL	Romosozumab 90 mg/mL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	46[5]	110[6]	116[7]	
Units: percent change				
least squares mean (confidence interval 95%)	0 (-0.9 to 0.8)	3.9 (3.4 to 4.4)	3.4 (2.9 to 4)	

Notes:

[5] - Subjects with values at baseline and at month 6

[6] - Subjects with values at baseline and at month 6

[7] - Subjects with values at baseline and at month 6

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Femoral Neck BMD

End point title	Percent Change From Baseline in Femoral Neck BMD

End point description:

Femoral neck BMD was measured using DXA. The analysis was based on ANCOVA model adjusting for treatment, and baseline femoral neck BMD T score.

End point type	Secondary

End point timeframe:

Baseline and month 6

End point values	Placebo	Romosozumab 70 mg/mL	Romosozumab 90 mg/mL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	46[8]	110[9]	116[10]	
Units: percent change				
least squares mean (confidence interval 95%)	-0.5 (-1.5 to 0.5)	3.1 (2.5 to 3.8)	2.6 (2 to 3.3)	

Notes:

[8] - Subjects with values at baseline and month 6

[9] - Subjects with values at baseline and month 6

[10] - Subjects with values at baseline and month 6

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in N-Terminal Propeptide Type 1 Procollagen (P1NP)

End point title	Percent Change From Baseline in N-Terminal Propeptide Type 1 Procollagen (P1NP)

End point description:

End point type	Secondary

End point timeframe:

Baseline, month 1, month 3 and month 6

End point values	Placebo	Romosozumab 70 mg/mL	Romosozumab 90 mg/mL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	51[11]	115[12]	120[13]	
Units: percent change				
median (inter-quartile range (Q1-Q3))				
Month 1 (n = 51, 111, 116)	2 (-5.797 to 16.129)	96.296 (67.143 to 159.341)	97.435 (69.259 to 126.179)	
Month 3 (n = 48, 110, 115)	-9.601 (-21.503 to 2.922)	23.96 (-1.587 to 46.667)	16.216 (-10.39 to 50)	
Month 6 (n = 45, 102, 110)	-12.5 (-27.5 to 14.286)	-2.885 (-28.07 to 18.421)	-3.604 (-22.222 to 27.273)	

Notes:

[11] - Subjects with values at baseline and at ≥ 1 post-baseline visit

[12] - Subjects with values at baseline and at ≥ 1 post-baseline visit

[13] - Subjects with values at baseline and at ≥ 1 post-baseline visit

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Serum C-Telopeptide (CTX)

End point title	Percent Change From Baseline in Serum C-Telopeptide (CTX)

End point description:

End point type	Secondary

End point timeframe:

Baseline, month 1, month 3 and month 6

End point values	Placebo	Romosozumab 70 mg/mL	Romosozumab 90 mg/mL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	51[14]	115[15]	120[16]	
Units: percent change				
median (inter-quartile range (Q1-Q3))				
Month 1 (n = 51, 111, 117)	0.282 (-16.183 to 12.874)	-23.158 (-42.943 to -9.967)	-21.456 (-35.602 to -7.246)	
Month 3 (n = 48, 110, 116)	-5.687 (-20.666 to 15.566)	-11.219 (-35.206 to 9.484)	-5.473 (-24.139 to 26.386)	
Month 6 (n = 45, 108, 114)	-8.12 (-26.935 to 10.059)	-25.78 (-43.573 to -8.216)	-17.305 (-37.566 to 6.405)	

Notes:

[14] - Subjects with values at baseline and at ≥ 1 post-baseline visit.

[15] - Subjects with values at baseline and at ≥ 1 post-baseline visit.

[16] - Subjects with values at baseline and at ≥ 1 post-baseline visit.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse events are reported from the first dose of study drug until 90 days after last dose (9 months overall).	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	Placebo 70 mg/mL
Reporting group description:	
Participants received matching placebo administered as 3 SC injections of 1.0 mL every month for 6 months.	
Reporting group title	Placebo 90 mg/mL
Reporting group description:	
Participants received matching placebo administered as 2 subcutaneous (SC) injections of 1.17 mL every month for 6 months.	
Reporting group title	Romosozumab 70 mg/mL
Reporting group description:	
Participants received 210 mg romosozumab monthly, administered as 3 subcutaneous 1 mL injections of a 70 mg/mL solution, for 6 months	
Reporting group title	Romosozumab 90 mg/mL
Reporting group description:	
Participants received 210 mg romosozumab monthly, administered as 2 subcutaneous 1.17 mL injections of a 90 mg/mL solution, for 6 months.	

Serious adverse events	Placebo 70 mg/mL	Placebo 90 mg/mL	Romosozumab 70 mg/mL
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 26 (15.38%)	2 / 26 (7.69%)	7 / 119 (5.88%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Medullary thyroid cancer			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine cancer			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Carbon monoxide poisoning			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Patella fracture			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arterial rupture			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Umbilical hernia repair			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyneuropathy			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retrograde amnesia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Coagulopathy			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			

subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis noninfective			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mesenteric artery embolism			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Spinal deformity			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal osteoarthritis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Vertebral lesion			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis perforated			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Romosozumab 90 mg/mL		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 123 (2.44%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Basal cell carcinoma			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Medullary thyroid cancer			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Uterine cancer			

subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Carbon monoxide poisoning			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Femoral neck fracture			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Humerus fracture			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Overdose			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Patella fracture			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Arterial rupture			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Cardiac failure			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Umbilical hernia repair			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Polyneuropathy			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Retrograde amnesia			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Coagulopathy			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Appendicitis noninfective			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mesenteric artery embolism			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Spinal deformity			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal osteoarthritis			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vertebral lesion			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Infections and infestations			
Appendicitis perforated			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo 70 mg/mL	Placebo 90 mg/mL	Romosozumab 70 mg/mL
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 26 (65.38%)	11 / 26 (42.31%)	62 / 119 (52.10%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Thyroid neoplasm			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Basal cell carcinoma			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Hot flush			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Hypertension			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	3 / 119 (2.52%)
occurrences (all)	1	0	3
Hypertensive angiopathy			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Phlebitis			

subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Varicose vein			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	1	0	1
General disorders and administration site conditions			
Administration site erythema			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Administration site reaction			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Asthenia			
subjects affected / exposed	0 / 26 (0.00%)	2 / 26 (7.69%)	4 / 119 (3.36%)
occurrences (all)	0	5	4
Chest pain			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	1	0	0
Cyst			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Generalised oedema			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Injection site erythema			

subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	2 / 119 (1.68%)
occurrences (all)	0	0	3
Injection site hypersensitivity			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	2
Injection site inflammation			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Injection site pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	7 / 119 (5.88%)
occurrences (all)	0	0	16
Injection site swelling			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Local swelling			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Polyp			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Hypersensitivity			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	1	0	0
Seasonal allergy			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1

Reproductive system and breast disorders			
Breast mass			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Breast swelling			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	1 / 119 (0.84%)
occurrences (all)	0	2	1
Emphysema			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Respiratory tract congestion			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	0 / 119 (0.00%)
occurrences (all)	0	1	0
Sinus congestion			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Neurosis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	0 / 119 (0.00%)
occurrences (all)	0	1	0
Investigations			

Blood glucose abnormal			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Blood potassium increased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Smear cervix abnormal			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Thyroid gland scan abnormal			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	1	0	0
Thyroxine increased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Tri-iodothyronine free increased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Ultrasound thyroid abnormal			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 26 (7.69%)	0 / 26 (0.00%)	2 / 119 (1.68%)
occurrences (all)	2	0	2
Contusion			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	3 / 119 (2.52%)
occurrences (all)	0	0	6
Forearm fracture			

subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Foot fracture			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Hand fracture			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Head injury			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Ligament injury			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Ligament sprain			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	1	0	1
Meniscus injury			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Neck injury			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	2
Patella fracture			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Radius fracture			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	1	0	1
Spinal fracture			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Tooth fracture			

subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	2 / 119 (1.68%)
occurrences (all)	0	0	2
Arrhythmia supraventricular			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Mitral valve incompetence			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Palpitations			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	1	0	1
Tricuspid valve incompetence			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Ventricular arrhythmia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Nervous system disorders			
Balance disorder			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Cerebrovascular disorder			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	1 / 119 (0.84%)
occurrences (all)	0	1	1
Cerebrovascular insufficiency			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Dizziness			

subjects affected / exposed	1 / 26 (3.85%)	1 / 26 (3.85%)	3 / 119 (2.52%)
occurrences (all)	1	1	3
Headache			
subjects affected / exposed	3 / 26 (11.54%)	0 / 26 (0.00%)	2 / 119 (1.68%)
occurrences (all)	3	0	2
Hypoaesthesia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	0 / 119 (0.00%)
occurrences (all)	0	1	0
Sciatica			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Vertebrobasilar insufficiency			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	1	0	0
Leukopenia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	1	0	0
Lymphadenopathy			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Ear discomfort			

subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Ear disorder			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	2	0	0
Tinnitus			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	2	0	0
Vertigo			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	2
Eye disorders			
Cataract			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	1 / 119 (0.84%)
occurrences (all)	0	1	2
Abdominal pain upper			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	2 / 119 (1.68%)
occurrences (all)	1	0	2
Aphthous stomatitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Chronic gastritis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	1	0	1
Diarrhoea			

subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	3 / 119 (2.52%)
occurrences (all)	0	1	3
Diverticulum intestinal			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Erosive oesophagitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Faeces discoloured			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Gastric ulcer			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Gastritis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	1 / 119 (0.84%)
occurrences (all)	0	1	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	2 / 119 (1.68%)
occurrences (all)	0	0	2
Gingival swelling			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Haemorrhoids			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	1	0	0
Inguinal hernia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Irritable bowel syndrome			

subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Large intestine polyp			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	2 / 119 (1.68%)
occurrences (all)	0	0	2
Nausea			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	2 / 119 (1.68%)
occurrences (all)	1	0	2
Pancreatitis chronic			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	0 / 119 (0.00%)
occurrences (all)	0	1	0
Peptic ulcer			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Periodontal disease			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Proctitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Salivary gland calculus			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Hepatic steatosis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0

Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Angioedema			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Dermatitis allergic			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	1 / 119 (0.84%)
occurrences (all)	0	1	1
Eczema			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Pruritus generalised			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Rash macular			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Skin lesion			

subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	0 / 119 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Nephrolithiasis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	2 / 119 (1.68%)
occurrences (all)	0	0	2
Renal colic			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Renal cyst			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Renal pain			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	0 / 119 (0.00%)
occurrences (all)	0	2	0
Urinary tract inflammation			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	2 / 119 (1.68%)
occurrences (all)	0	0	2
Thyroiditis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	1 / 26 (3.85%)	1 / 26 (3.85%)	1 / 119 (0.84%)
occurrences (all)	1	1	1
Arthralgia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	4 / 119 (3.36%)
occurrences (all)	0	2	4
Bone pain			
subjects affected / exposed	0 / 26 (0.00%)	2 / 26 (7.69%)	2 / 119 (1.68%)
occurrences (all)	0	2	2
Exostosis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Intervertebral disc disorder			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Joint stiffness			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	0 / 119 (0.00%)
occurrences (all)	0	1	0
Lordosis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	0 / 119 (0.00%)
occurrences (all)	0	1	0
Muscle contracture			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	1	0	1
Muscular weakness			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	3 / 119 (2.52%)
occurrences (all)	0	0	3
Osteoarthritis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	2 / 119 (1.68%)
occurrences (all)	0	1	2

Pain in extremity			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	2 / 119 (1.68%)
occurrences (all)	1	0	3
Spinal deformity			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Spinal osteoarthritis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	4 / 119 (3.36%)
occurrences (all)	1	0	4
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	2 / 119 (1.68%)
occurrences (all)	1	0	2
Ear infection bacterial			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Ear infection viral			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Gastroenteritis viral			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Genitourinary chlamydia infection			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	1	0	0
Gingivitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Helicobacter infection			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			

subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Infection			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Influenza			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	3 / 26 (11.54%)	0 / 26 (0.00%)	9 / 119 (7.56%)
occurrences (all)	4	0	10
Laryngitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Onychomycosis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Pharyngitis bacterial			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Pneumonia bacterial			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Pulpitis dental			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			

subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection viral			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	0 / 119 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	1	0	0
Tonsillitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 26 (3.85%)	2 / 26 (7.69%)	1 / 119 (0.84%)
occurrences (all)	1	2	1
Upper respiratory tract infection bacterial			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	1 / 119 (0.84%)
occurrences (all)	0	2	2
Urinary tract infection bacterial			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Vaginal infection			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	2 / 119 (1.68%)
occurrences (all)	0	0	2
Metabolism and nutrition disorders			
Hypercholesterolaemia			

subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	1	0	0
Hyperlipidaemia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Increased appetite			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1
Obesity			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 119 (0.00%)
occurrences (all)	0	0	0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 119 (0.84%)
occurrences (all)	0	0	1

Non-serious adverse events	Romosozumab 90 mg/mL		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	71 / 123 (57.72%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Thyroid neoplasm			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	2		
Basal cell carcinoma			
subjects affected / exposed	2 / 123 (1.63%)		
occurrences (all)	2		
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Hot flush			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	3 / 123 (2.44%)		
occurrences (all)	3		
Hypertensive angiopathy			

subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Phlebitis			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	2		
Varicose vein			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Administration site erythema			
subjects affected / exposed	2 / 123 (1.63%)		
occurrences (all)	4		
Administration site reaction			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Asthenia			
subjects affected / exposed	4 / 123 (3.25%)		
occurrences (all)	5		
Chest pain			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Cyst			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Generalised oedema			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Influenza like illness			

subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Injection site erythema			
subjects affected / exposed	7 / 123 (5.69%)		
occurrences (all)	23		
Injection site hypersensitivity			
subjects affected / exposed	2 / 123 (1.63%)		
occurrences (all)	2		
Injection site inflammation			
subjects affected / exposed	2 / 123 (1.63%)		
occurrences (all)	2		
Injection site pain			
subjects affected / exposed	3 / 123 (2.44%)		
occurrences (all)	15		
Injection site swelling			
subjects affected / exposed	4 / 123 (3.25%)		
occurrences (all)	5		
Local swelling			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Polyp			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Hypersensitivity			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		

Seasonal allergy			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Breast mass			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Breast swelling			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Cough			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Emphysema			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Respiratory tract congestion			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Rhinitis allergic			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Sinus congestion			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Neurosis			

subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Investigations			
Blood glucose abnormal			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Blood potassium increased			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Smear cervix abnormal			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Thyroid gland scan abnormal			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Thyroxine increased			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Tri-iodothyronine free increased			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Weight increased			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Ultrasound thyroid abnormal			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 123 (1.63%)		
occurrences (all)	4		
Contusion			

subjects affected / exposed	3 / 123 (2.44%)			
occurrences (all)	6			
Forearm fracture				
subjects affected / exposed	0 / 123 (0.00%)			
occurrences (all)	0			
Foot fracture				
subjects affected / exposed	1 / 123 (0.81%)			
occurrences (all)	1			
Hand fracture				
subjects affected / exposed	1 / 123 (0.81%)			
occurrences (all)	1			
Head injury				
subjects affected / exposed	0 / 123 (0.00%)			
occurrences (all)	0			
Ligament injury				
subjects affected / exposed	0 / 123 (0.00%)			
occurrences (all)	0			
Ligament sprain				
subjects affected / exposed	2 / 123 (1.63%)			
occurrences (all)	2			
Meniscus injury				
subjects affected / exposed	0 / 123 (0.00%)			
occurrences (all)	0			
Neck injury				
subjects affected / exposed	0 / 123 (0.00%)			
occurrences (all)	0			
Patella fracture				
subjects affected / exposed	0 / 123 (0.00%)			
occurrences (all)	0			
Procedural pain				
subjects affected / exposed	0 / 123 (0.00%)			
occurrences (all)	0			
Radius fracture				
subjects affected / exposed	1 / 123 (0.81%)			
occurrences (all)	1			
Spinal fracture				

subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Tooth fracture			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Arrhythmia supraventricular			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Mitral valve incompetence			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Atrial fibrillation			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Palpitations			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Tricuspid valve incompetence			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Ventricular arrhythmia			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Balance disorder			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Cerebrovascular disorder			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Cerebrovascular insufficiency			

subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	2 / 123 (1.63%)		
occurrences (all)	2		
Hypoaesthesia			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Paraesthesia			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Migraine			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Sciatica			
subjects affected / exposed	3 / 123 (2.44%)		
occurrences (all)	3		
Tremor			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Vertebrobasilar insufficiency			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Leukopenia			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Lymphadenopathy			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		

Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Ear disorder			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Tinnitus			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Vertigo			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Eye disorders			
Cataract			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Aphthous stomatitis			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Chronic gastritis			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Diarrhoea			

subjects affected / exposed	0 / 123 (0.00%)			
occurrences (all)	0			
Diverticulum intestinal				
subjects affected / exposed	0 / 123 (0.00%)			
occurrences (all)	0			
Dyspepsia				
subjects affected / exposed	0 / 123 (0.00%)			
occurrences (all)	0			
Erosive oesophagitis				
subjects affected / exposed	1 / 123 (0.81%)			
occurrences (all)	1			
Faeces discoloured				
subjects affected / exposed	1 / 123 (0.81%)			
occurrences (all)	1			
Gastric ulcer				
subjects affected / exposed	1 / 123 (0.81%)			
occurrences (all)	1			
Gastritis				
subjects affected / exposed	1 / 123 (0.81%)			
occurrences (all)	1			
Gastrooesophageal reflux disease				
subjects affected / exposed	1 / 123 (0.81%)			
occurrences (all)	1			
Gingival swelling				
subjects affected / exposed	1 / 123 (0.81%)			
occurrences (all)	2			
Haemorrhoidal haemorrhage				
subjects affected / exposed	0 / 123 (0.00%)			
occurrences (all)	0			
Haemorrhoids				
subjects affected / exposed	1 / 123 (0.81%)			
occurrences (all)	1			
Inguinal hernia				
subjects affected / exposed	1 / 123 (0.81%)			
occurrences (all)	1			
Irritable bowel syndrome				

subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Large intestine polyp			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Pancreatitis chronic			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Peptic ulcer			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Periodontal disease			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Proctitis			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Salivary gland calculus			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Toothache			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Hepatic steatosis			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		

Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Angioedema			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Dermatitis allergic			
subjects affected / exposed	3 / 123 (2.44%)		
occurrences (all)	3		
Eczema			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	12		
Erythema			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Hyperhidrosis			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	10		
Pruritus generalised			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	2		
Rash			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	6		
Rash macular			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	2		
Rash pruritic			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Skin lesion			

subjects affected / exposed occurrences (all) Urticaria subjects affected / exposed occurrences (all)	2 / 123 (1.63%) 11 0 / 123 (0.00%) 0		
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all) Nephrolithiasis subjects affected / exposed occurrences (all) Renal colic subjects affected / exposed occurrences (all) Renal cyst subjects affected / exposed occurrences (all) Renal pain subjects affected / exposed occurrences (all) Urinary tract inflammation subjects affected / exposed occurrences (all)	 1 / 123 (0.81%) 1 1 / 123 (0.81%) 1 1 / 123 (0.81%) 1 1 / 123 (0.81%) 1 0 / 123 (0.00%) 0 0 / 123 (0.00%) 0		
Endocrine disorders Hyperthyroidism subjects affected / exposed occurrences (all) Hypothyroidism subjects affected / exposed occurrences (all) Thyroiditis subjects affected / exposed occurrences (all)	 1 / 123 (0.81%) 1 0 / 123 (0.00%) 0 0 / 123 (0.00%) 0		
Musculoskeletal and connective tissue disorders			

Back pain				
subjects affected / exposed	0 / 123 (0.00%)			
occurrences (all)	0			
Arthralgia				
subjects affected / exposed	6 / 123 (4.88%)			
occurrences (all)	10			
Bone pain				
subjects affected / exposed	2 / 123 (1.63%)			
occurrences (all)	2			
Exostosis				
subjects affected / exposed	1 / 123 (0.81%)			
occurrences (all)	1			
Intervertebral disc disorder				
subjects affected / exposed	1 / 123 (0.81%)			
occurrences (all)	1			
Joint stiffness				
subjects affected / exposed	0 / 123 (0.00%)			
occurrences (all)	0			
Lordosis				
subjects affected / exposed	0 / 123 (0.00%)			
occurrences (all)	0			
Muscle contracture				
subjects affected / exposed	1 / 123 (0.81%)			
occurrences (all)	1			
Musculoskeletal pain				
subjects affected / exposed	2 / 123 (1.63%)			
occurrences (all)	2			
Muscular weakness				
subjects affected / exposed	1 / 123 (0.81%)			
occurrences (all)	1			
Myalgia				
subjects affected / exposed	3 / 123 (2.44%)			
occurrences (all)	4			
Osteoarthritis				
subjects affected / exposed	6 / 123 (4.88%)			
occurrences (all)	6			

Pain in extremity			
subjects affected / exposed	4 / 123 (3.25%)		
occurrences (all)	8		
Spinal deformity			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Spinal pain			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Spinal osteoarthritis			
subjects affected / exposed	2 / 123 (1.63%)		
occurrences (all)	2		
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 123 (2.44%)		
occurrences (all)	3		
Ear infection bacterial			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Ear infection viral			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Gastroenteritis viral			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Genitourinary chlamydia infection			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Gingivitis			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Helicobacter infection			
subjects affected / exposed	2 / 123 (1.63%)		
occurrences (all)	2		
Herpes zoster			

subjects affected / exposed	0 / 123 (0.00%)			
occurrences (all)	0			
Infection				
subjects affected / exposed	0 / 123 (0.00%)			
occurrences (all)	0			
Influenza				
subjects affected / exposed	0 / 123 (0.00%)			
occurrences (all)	0			
Nasopharyngitis				
subjects affected / exposed	19 / 123 (15.45%)			
occurrences (all)	21			
Laryngitis				
subjects affected / exposed	0 / 123 (0.00%)			
occurrences (all)	0			
Onychomycosis				
subjects affected / exposed	1 / 123 (0.81%)			
occurrences (all)	1			
Oral herpes				
subjects affected / exposed	1 / 123 (0.81%)			
occurrences (all)	1			
Pharyngitis				
subjects affected / exposed	2 / 123 (1.63%)			
occurrences (all)	2			
Pharyngitis bacterial				
subjects affected / exposed	0 / 123 (0.00%)			
occurrences (all)	0			
Pneumonia				
subjects affected / exposed	0 / 123 (0.00%)			
occurrences (all)	0			
Pneumonia bacterial				
subjects affected / exposed	0 / 123 (0.00%)			
occurrences (all)	0			
Pulpitis dental				
subjects affected / exposed	1 / 123 (0.81%)			
occurrences (all)	1			
Respiratory tract infection				

subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Respiratory tract infection viral			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	4 / 123 (3.25%)		
occurrences (all)	4		
Tonsillitis			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	2 / 123 (1.63%)		
occurrences (all)	2		
Upper respiratory tract infection bacterial			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	7 / 123 (5.69%)		
occurrences (all)	7		
Urinary tract infection bacterial			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Vaginal infection			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Viral upper respiratory tract infection			
subjects affected / exposed	3 / 123 (2.44%)		
occurrences (all)	3		
Metabolism and nutrition disorders			
Hypercholesterolaemia			

subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Hyperlipidaemia			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Increased appetite			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		
Obesity			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 123 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 September 2013	The protocol was amended to include the following changes: - To include an additional assessment for formation of antiromosozumab antibodies at the month 1 study visit. This additional assessment allowed a more comprehensive characterization of the antiromosozumab antibody response. - The eligibility criteria were modified to allow participation of a wider range of subjects. Specifically, the minimal age was lowered from 60 to 55 years and for exclusionary medications, the protocol-mandated off-treatment times were revised. Similarly, the use of vitamin K (and analogs) for the treatment of osteoporosis, and the use of activated vitamin D were added to the on-study excluded treatments list. - To account for the imprecision of serum calcium laboratory measurements, retesting of serum calcium was permitted within the screening window if the initial test indicated an elevated level of serum calcium within 1.1x the upper limit of normal set by the central laboratory. - It was clarified that if a subject was rescreened for serum 25-hydroxyvitamin D level, they were not required to reconsent for the rescreening period. - Expectations for serious adverse event reporting were defined for the time after the protocol-mandated reporting period ended. - Analysis detail pertaining to the assessment of antiromosozumab antibodies was modified to reflect the statistical analysis plan.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported