Clinical trial results:
Multicenter, Randomized, Double-blind, Placebo-controlled Study to Compare the Efficacy and Safety of Romosozumab With Placebo in Men With Osteoporosis

Summary

EudraCT number	2013-005551-32
Trial protocol	CZ BE DK PL
Global end of trial date	20 April 2016

Results information

Result version number	v1 (current)
This version publication date	13 April 2017
First version publication date	13 April 2017

Trial information

Trial identification

Sponsor protocol code	20110174

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02186171
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, 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	20 April 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 April 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the effect of treatment with romosozumab for 12 months compared with placebo on percent changes from baseline in bone mineral density (BMD) at the lumbar spine as assessed by dual-energy x-ray absorptiometry (DXA) in men with osteoporosis.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) and applicable regulatory requirements.
All subjects provided written informed consent before undergoing any study-related procedures, including screening procedures.
The study protocol, amendments, and the informed consent form (ICF) were reviewed by the Institutional Review Boards (IRBs) and Independent Ethics Committees (IECs). No subjects were recruited into the study and no investigational product (IP) was shipped until the IRB/IEC gave written approval of the protocol and ICF and Amgen received copies of these approvals.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 June 2014
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: 47
Country: Number of subjects enrolled	Czech Republic: 27
Country: Number of subjects enrolled	Denmark: 35
Country: Number of subjects enrolled	Belgium: 18
Country: Number of subjects enrolled	Russian Federation: 20
Country: Number of subjects enrolled	Switzerland: 15
Country: Number of subjects enrolled	Colombia: 35
Country: Number of subjects enrolled	Japan: 27
Country: Number of subjects enrolled	United States: 21
Worldwide total number of subjects	245
EEA total number of subjects	127

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)	42
From 65 to 84 years	197
85 years and over	6

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 31 centers in Europe, North America, Latin America, and Japan. Participants were enrolled from 16 June 2014 to 27 January 2015.

Pre-assignment

Screening details:

Participants were randomized in a 2:1 ratio to receive 210 mg romosozumab or matched placebo in a blinded fashion for the duration of the 12-month treatment period. Randomization was stratified by geographic region (Europe, North America, Latin America, and Japan).

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received placebo subcutaneous injections once a month (QM) for 12 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

Arm description:

Participants received 210 mg romosozumab administered by subcutaneous injection once a month for 12 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 by subcutaneous injection once a month

Number of subjects in period 1	Placebo	Romosozumab
Started	82	163
Received Treatment	81	163
Completed	78	148
Not completed	4	15
Consent withdrawn by subject	1	9
Death	1	2
Lost to follow-up	2	2
Protocol-specified criteria	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo subcutaneous injections once a month (QM) for 12 months.	
Reporting group title	Romosozumab
Reporting group description:	
Participants received 210 mg romosozumab administered by subcutaneous injection once a month for 12 months.	

Reporting group values	Placebo	Romosozumab	Total
Number of subjects	82	163	245
Age Categorical			
Units: Subjects			
Adults (18-64 years)	11	31	42
From 65-74 years	42	62	104
75 years and over	29	70	99
Age Continuous			
Units: years			
arithmetic mean	71.5	72.4	
standard deviation	± 6.9	± 7.4	-
Gender Categorical			
Units: Subjects			
Female	0	0	0
Male	82	163	245
Race			
Units: Subjects			
White	60	120	180
Asian	9	18	27
Black or African American	0	1	1
Other	13	23	36
Multiple	0	1	1
Geographic Region			
Units: Subjects			
Europe	54	108	162
Japan	9	18	27
Latin America	12	23	35
North America	7	14	21
Lumbar Spine 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	-2.33	-2.22	
standard deviation	± 1.41	± 1.19	-
Total Hip BMD T-score			
Units: T-score			
arithmetic mean	-1.92	-1.92	

standard deviation	± 0.65	± 0.59	-
Femoral Neck BMD T-score			
Units: T-score			
arithmetic mean	-2.3	-2.34	
standard deviation	± 0.52	± 0.52	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received placebo subcutaneous injections once a month (QM) for 12 months.	
Reporting group title	Romosozumab
Reporting group description:	
Participants received 210 mg romosozumab administered by subcutaneous injection once a month for 12 months.	

Primary: Percent Change From Baseline in Lumbar Spine Bone Mineral Density (BMD) at Month 12

End point title	Percent Change From Baseline in Lumbar Spine Bone Mineral Density (BMD) at Month 12
End point description:	
Lumbar spine bone mineral density (BMD) was measured by dual x-ray absorptiometry (DXA). DXA scans were analyzed by a central imaging center. This endpoint was analyzed using the primary efficacy analysis subset which includes all randomized participants who had a baseline DXA BMD measurement and at least 1 post-baseline DXA BMD measurement at the lumbar spine; last observation carried forward (LOCF) imputation was used.	
End point type	Primary
End point timeframe:	
Baseline and month 12	

End point values	Placebo	Romosozumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	79	157		
Units: percent change				
least squares mean (standard error)	1.2 (± 0.5)	12.1 (± 0.5)		

Statistical analyses

Statistical analysis title	Primary Analysis
Comparison groups	Placebo v Romosozumab
Number of subjects included in analysis	236
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [1]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	10.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	9.6
upper limit	12.2
Variability estimate	Standard error of the mean
Dispersion value	0.6

Notes:

[1] - ANCOVA model adjusting for treatment, baseline BMD value, machine type, machine type-by-baseline BMD value, baseline testosterone level, geographic region, and using a variance structure allowing for heterogeneity between treatment groups.

Secondary: Percent Change from Baseline in BMD at the Total Hip at Month 12

End point title	Percent Change from Baseline in BMD at the Total Hip at Month 12

End point description:

Total hip bone mineral density (BMD) was measured by dual x-ray absorptiometry (DXA). DXA scans were analyzed by a central imaging center.
This endpoint was analyzed using the primary efficacy analysis subset which includes all randomized participants who had a baseline DXA BMD measurement and at least 1 post-baseline DXA BMD measurement at the total hip; LOCF imputation was used.

End point type	Secondary

End point timeframe:

Baseline and month 12

End point values	Placebo	Romosozumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	79	158		
Units: percent change				
least squares mean (standard error)	-0.5 (± 0.3)	2.5 (± 0.2)		

Statistical analyses

Statistical analysis title	Primary Analysis
Comparison groups	Placebo v Romosozumab
Number of subjects included in analysis	237
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	< 0.0001 [3]
Method	ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.3
upper limit	3.7

Variability estimate	Standard error of the mean
Dispersion value	0.4

Notes:

[2] - The Hochberg procedure was employed to control the overall type 1 error for the percent change from baseline at 12 months in total hip and femoral neck to maintain the overall significance level at 0.05.
[3] - ANCOVA model adjusting for treatment, baseline BMD value, machine type, machine type-by-baseline BMD value, baseline testosterone level, geographic region, and using a variance structure allowing for heterogeneity between treatment groups.

Secondary: Percent Change from Baseline in BMD at the Femoral Neck at Month 12

End point title	Percent Change from Baseline in BMD at the Femoral Neck at Month 12

End point description:

Femoral neck bone mineral density (BMD) was measured by dual x-ray absorptiometry (DXA). DXA scans were analyzed by a central imaging center.
This endpoint was analyzed using the primary efficacy analysis subset which includes all randomized participants who had a baseline DXA BMD measurement and at least 1 post-baseline DXA BMD measurement at the femoral neck; LOCF imputation was used.

End point type	Secondary

End point timeframe:

Baseline and month 12

End point values	Placebo	Romosozumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	79	158		
Units: percent change				
least squares mean (standard error)	-0.2 (± 0.4)	2.2 (± 0.4)		

Statistical analyses

Statistical analysis title	Primary Analysis
Comparison groups	Placebo v Romosozumab
Number of subjects included in analysis	237
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	< 0.0001 [5]
Method	ANCOVA
Parameter estimate	Treatment Difference
Point estimate	2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.5
upper limit	3.3
Variability estimate	Standard error of the mean
Dispersion value	0.5

Notes:

[4] - The Hochberg procedure was employed to control the overall type 1 error for the percent change from baseline at 12 months in total hip and femoral neck to maintain the overall significance level at 0.05.
[5] - ANCOVA model adjusting for treatment, baseline BMD value, machine type, machine type-by-baseline BMD value, baseline testosterone level, geographic region, and using a variance structure allowing for heterogeneity between treatment groups.

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

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

End point description:

Lumbar spine bone mineral density (BMD) was measured by dual x-ray absorptiometry (DXA). DXA scans were analyzed by a central imaging center.
This endpoint was analyzed using the primary efficacy analysis subset with available data at baseline and month 6.

End point type	Secondary

End point timeframe:

Baseline and month 6

End point values	Placebo	Romosozumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	156		
Units: percent change				
least squares mean (standard error)	0.3 (± 0.4)	9 (± 0.4)		

Statistical analyses

Statistical analysis title	Primary Analysis
Comparison groups	Placebo v Romosozumab
Number of subjects included in analysis	234
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	< 0.0001 [7]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	8.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.6
upper limit	9.7
Variability estimate	Standard error of the mean
Dispersion value	0.5

Notes:

[6] - The Hochberg procedure was employed to control the overall type 1 error for the percent change from baseline at 6 months at the lumbar spine, total hip and femoral neck BMD in order to maintain the overall significance level at 0.05.
[7] - ANCOVA model adjusting for treatment, baseline BMD value, machine type, machine type-by-

baseline BMD value, baseline testosterone level, geographic region, and using a variance structure allowing for heterogeneity between treatment groups.

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

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

End point description:

Bone mineral density (BMD) was measured by dual x-ray absorptiometry (DXA). DXA scans were analyzed by a central imaging center.
This endpoint was analyzed using the primary efficacy analysis subset with available data at baseline and month 6.

End point type	Secondary

End point timeframe:

Baseline and month 6

End point values	Placebo	Romosozumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	157		
Units: percent change				
least squares mean (standard error)	0.2 (± 0.2)	1.6 (± 0.2)		

Statistical analyses

Statistical analysis title	Primary Analysis
Comparison groups	Placebo v Romosozumab
Number of subjects included in analysis	235
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	< 0.0001 [9]
Method	ANCOVA
Parameter estimate	LS Mean Treatment Difference
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	2
Variability estimate	Standard error of the mean
Dispersion value	0.3

Notes:

[8] - The Hochberg procedure was employed to control the overall type 1 error for the percent change from baseline at 6 months at the lumbar spine, total hip and femoral neck BMD in order to maintain the overall significance level at 0.05.
[9] - ANCOVA model adjusting for treatment, baseline BMD value, machine type, machine type-by-baseline BMD value, baseline testosterone level, geographic region, and using a variance structure allowing for heterogeneity between treatment groups.

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

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

End point description:

Bone mineral density (BMD) was measured by dual x-ray absorptiometry (DXA). DXA scans were analyzed by a central imaging center.
This endpoint was analyzed using the primary efficacy analysis subset with available data at baseline and month 6.

End point type	Secondary

End point timeframe:

Baseline and month 6

End point values	Placebo	Romosozumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	157		
Units: percent change				
least squares mean (standard error)	0 (± 0.4)	1.2 (± 0.3)		

Statistical analyses

Statistical analysis title	Primary Analysis
Comparison groups	Placebo v Romosozumab
Number of subjects included in analysis	235
Analysis specification	Pre-specified
Analysis type	superiority[10]
P-value	= 0.0033 [11]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	2.1
Variability estimate	Standard error of the mean
Dispersion value	0.4

Notes:

[10] - The Hochberg procedure was employed to control the overall type 1 error for the percent change from baseline at 6 months at the lumbar spine, total hip and femoral neck BMD in order to maintain the overall significance level at 0.05.
[11] - ANCOVA model adjusting for treatment, baseline BMD value, machine type, machine type-by-baseline BMD value, baseline testosterone level, geographic region, and using a variance structure allowing for heterogeneity between treatment groups.

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
15 months	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups	
Reporting group title	Romosozumab
Reporting group description:	
Participants received 210 mg romosozumab administered by subcutaneous injection once a month for 12 months.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo subcutaneous injections once a month (QM) for 12 months.	

Serious adverse events	Romosozumab	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 163 (14.11%)	10 / 81 (12.35%)	
number of deaths (all causes)	2	1	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oropharyngeal cancer			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Anaemia postoperative			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			

subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (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 / 163 (0.61%)	0 / 81 (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	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina unstable			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			

subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	1 / 163 (0.61%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac valve disease			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	2 / 163 (1.23%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wolff-Parkinson-White syndrome			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (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 arteriosclerosis			

subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral ischaemia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia Alzheimer's type			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic stroke			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lacunar infarction			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			

subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular encephalopathy			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 163 (0.61%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Implant site haematoma			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 163 (0.61%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Intra-abdominal haemorrhage			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Emphysema			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			

Osteoarthritis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis perforated			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (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	2 / 163 (1.23%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Romosozumab	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	122 / 163 (74.85%)	65 / 81 (80.25%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	2 / 163 (1.23%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Benign lung neoplasm			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Benign neoplasm of adrenal gland			
subjects affected / exposed	0 / 163 (0.00%)	2 / 81 (2.47%)	
occurrences (all)	0	2	
Benign renal neoplasm			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Lipoma			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Paranasal sinus benign neoplasm			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Prostatic adenoma			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Seborrhoeic keratosis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Skin papilloma			

subjects affected / exposed	2 / 163 (1.23%)	0 / 81 (0.00%)	
occurrences (all)	3	0	
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 163 (0.00%)	2 / 81 (2.47%)	
occurrences (all)	0	2	
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Aortic dilatation			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	2	
Arteriosclerosis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Essential hypertension			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Haematoma			
subjects affected / exposed	3 / 163 (1.84%)	0 / 81 (0.00%)	
occurrences (all)	3	0	
Hypertension			
subjects affected / exposed	14 / 163 (8.59%)	5 / 81 (6.17%)	
occurrences (all)	17	5	
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Peripheral venous disease			
subjects affected / exposed	4 / 163 (2.45%)	0 / 81 (0.00%)	
occurrences (all)	4	0	
Subclavian artery stenosis			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Varicose vein			
subjects affected / exposed	1 / 163 (0.61%)	1 / 81 (1.23%)	
occurrences (all)	1	1	

Surgical and medical procedures			
Osteosynthesis			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Application site dermatitis			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Asthenia			
subjects affected / exposed	0 / 163 (0.00%)	2 / 81 (2.47%)	
occurrences (all)	0	2	
Chills			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Discomfort			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Drug withdrawal syndrome			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	3 / 163 (1.84%)	4 / 81 (4.94%)	
occurrences (all)	3	4	
Influenza like illness			
subjects affected / exposed	6 / 163 (3.68%)	0 / 81 (0.00%)	
occurrences (all)	6	0	
Injection site bruising			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Injection site erythema			
subjects affected / exposed	3 / 163 (1.84%)	1 / 81 (1.23%)	
occurrences (all)	5	1	
Injection site haematoma			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Injection site hypersensitivity			

subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Injection site induration			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Injection site pain			
subjects affected / exposed	4 / 163 (2.45%)	0 / 81 (0.00%)	
occurrences (all)	9	0	
Injection site pruritus			
subjects affected / exposed	1 / 163 (0.61%)	2 / 81 (2.47%)	
occurrences (all)	3	2	
Injection site swelling			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Local swelling			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Malaise			
subjects affected / exposed	2 / 163 (1.23%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 163 (0.61%)	1 / 81 (1.23%)	
occurrences (all)	2	1	
Immune system disorders			
Allergy to arthropod bite			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Drug hypersensitivity			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
House dust allergy			
subjects affected / exposed	2 / 163 (1.23%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Seasonal allergy			
subjects affected / exposed	1 / 163 (0.61%)	2 / 81 (2.47%)	
occurrences (all)	1	2	

Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Benign prostatic hyperplasia			
subjects affected / exposed	5 / 163 (3.07%)	0 / 81 (0.00%)	
occurrences (all)	5	0	
Breast pain			
subjects affected / exposed	0 / 163 (0.00%)	2 / 81 (2.47%)	
occurrences (all)	0	2	
Breast swelling			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Nipple disorder			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Prostatitis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Allergic pharyngitis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Asthma			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Bronchiectasis			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Chronic obstructive pulmonary disease			
subjects affected / exposed	2 / 163 (1.23%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Cough			
subjects affected / exposed	5 / 163 (3.07%)	1 / 81 (1.23%)	
occurrences (all)	5	1	

Dyspnoea			
subjects affected / exposed	1 / 163 (0.61%)	1 / 81 (1.23%)	
occurrences (all)	2	1	
Dyspnoea exertional			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Emphysema			
subjects affected / exposed	1 / 163 (0.61%)	1 / 81 (1.23%)	
occurrences (all)	1	1	
Epistaxis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	2 / 163 (1.23%)	1 / 81 (1.23%)	
occurrences (all)	2	1	
Productive cough			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Pulmonary embolism			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Pulmonary fibrosis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Rhinitis allergic			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Rhinorrhoea			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	2	
Psychiatric disorders			
Adjustment disorder with depressed mood			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Affective disorder			

subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Confusional state			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Depressed mood			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Depression			
subjects affected / exposed	2 / 163 (1.23%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Insomnia			
subjects affected / exposed	1 / 163 (0.61%)	1 / 81 (1.23%)	
occurrences (all)	1	1	
Personality change due to a general medical condition			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Restlessness			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Blood glucose increased			
subjects affected / exposed	2 / 163 (1.23%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Blood uric acid increased			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Cardiac murmur			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Heart rate irregular			

subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Vitamin D decreased			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Vitamin D increased			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Arthropod sting			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Chest injury			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Contusion			
subjects affected / exposed	0 / 163 (0.00%)	3 / 81 (3.70%)	
occurrences (all)	0	3	
Face injury			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Fall			
subjects affected / exposed	6 / 163 (3.68%)	2 / 81 (2.47%)	
occurrences (all)	7	4	
Head injury			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Joint injury			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Laceration			

subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Ligament sprain			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Lumbar vertebral fracture			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Meniscus injury			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Muscle strain			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Post procedural haematoma			
subjects affected / exposed	2 / 163 (1.23%)	1 / 81 (1.23%)	
occurrences (all)	2	1	
Post procedural haemorrhage			
subjects affected / exposed	1 / 163 (0.61%)	1 / 81 (1.23%)	
occurrences (all)	1	1	
Procedural pain			
subjects affected / exposed	8 / 163 (4.91%)	6 / 81 (7.41%)	
occurrences (all)	9	7	
Skin abrasion			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Tendon rupture			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Tooth fracture			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	3	
Congenital, familial and genetic disorders			
Hydrocele			

subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	2 / 163 (1.23%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Aortic valve incompetence			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Arteriosclerosis coronary artery			
subjects affected / exposed	1 / 163 (0.61%)	1 / 81 (1.23%)	
occurrences (all)	1	1	
Atrial fibrillation			
subjects affected / exposed	1 / 163 (0.61%)	1 / 81 (1.23%)	
occurrences (all)	1	1	
Atrial flutter			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Atrioventricular block first degree			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Cardiac failure chronic			
subjects affected / exposed	1 / 163 (0.61%)	1 / 81 (1.23%)	
occurrences (all)	1	1	
Extrasystoles			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Left atrial dilatation			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Mitral valve incompetence			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Myocardial ischaemia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	

Palpitations			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Supraventricular extrasystoles			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Supraventricular tachycardia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Ventricular extrasystoles			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
Cerebral arteriosclerosis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Cognitive disorder			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Disturbance in attention			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	5 / 163 (3.07%)	1 / 81 (1.23%)	
occurrences (all)	5	1	
Dysaesthesia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	10 / 163 (6.13%)	6 / 81 (7.41%)	
occurrences (all)	12	7	
Hypoaesthesia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
IIIrd nerve paralysis			

subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
IVth nerve paralysis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Loss of consciousness			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Migraine			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Paraesthesia			
subjects affected / exposed	2 / 163 (1.23%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Polyneuropathy			
subjects affected / exposed	1 / 163 (0.61%)	1 / 81 (1.23%)	
occurrences (all)	1	1	
Radicular syndrome			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Radiculopathy			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Sciatica			
subjects affected / exposed	2 / 163 (1.23%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Seizure			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Somnolence			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Syncope			
subjects affected / exposed	2 / 163 (1.23%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Transient ischaemic attack			

subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
VIth nerve paralysis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 163 (0.61%)	2 / 81 (2.47%)	
occurrences (all)	1	2	
Lymphadenopathy			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Vertigo			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Vertigo positional			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Arteriosclerotic retinopathy			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Blepharitis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Cataract			
subjects affected / exposed	4 / 163 (2.45%)	1 / 81 (1.23%)	
occurrences (all)	4	1	
Conjunctivitis allergic			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Ectropion			

subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Eye allergy			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Eye pain			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Glaucoma			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Macular degeneration			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Vision blurred			
subjects affected / exposed	1 / 163 (0.61%)	1 / 81 (1.23%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	2 / 163 (1.23%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Abdominal hernia			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Abdominal pain			
subjects affected / exposed	3 / 163 (1.84%)	0 / 81 (0.00%)	
occurrences (all)	3	0	
Abdominal pain upper			
subjects affected / exposed	3 / 163 (1.84%)	0 / 81 (0.00%)	
occurrences (all)	5	0	
Ascites			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Cheilitis			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	

Cheilosis			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Coeliac artery stenosis			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	9 / 163 (5.52%)	1 / 81 (1.23%)	
occurrences (all)	10	1	
Dental caries			
subjects affected / exposed	3 / 163 (1.84%)	0 / 81 (0.00%)	
occurrences (all)	3	0	
Diarrhoea			
subjects affected / exposed	6 / 163 (3.68%)	4 / 81 (4.94%)	
occurrences (all)	6	4	
Diverticulum			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Diverticulum intestinal			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
subjects affected / exposed	3 / 163 (1.84%)	3 / 81 (3.70%)	
occurrences (all)	4	4	
Eructation			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Functional gastrointestinal disorder			
subjects affected / exposed	2 / 163 (1.23%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Gastric ulcer			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Haemorrhagic erosive gastritis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	

Haemorrhoids			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Hiatus hernia			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Inguinal hernia			
subjects affected / exposed	2 / 163 (1.23%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Intestinal dilatation			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Irritable bowel syndrome			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Large intestine polyp			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Loose tooth			
subjects affected / exposed	0 / 163 (0.00%)	2 / 81 (2.47%)	
occurrences (all)	0	2	
Mesenteric artery stenosis			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	1 / 163 (0.61%)	1 / 81 (1.23%)	
occurrences (all)	1	1	
Odynophagia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Oesophagitis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Pancreatic cyst			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	

Periodontal disease			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Stomatitis			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Teeth brittle			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Toothache			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Truncus coeliacus thrombosis			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 163 (0.00%)	2 / 81 (2.47%)	
occurrences (all)	0	2	
Gallbladder polyp			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Hepatic cyst			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Hepatomegaly			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Actinic keratosis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Blister			

subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Dermatitis allergic			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Dermatitis contact			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Dry skin			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Ecchymosis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Eczema			
subjects affected / exposed	0 / 163 (0.00%)	2 / 81 (2.47%)	
occurrences (all)	0	2	
Erythema			
subjects affected / exposed	2 / 163 (1.23%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Hyperhidrosis			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Miliaria			
subjects affected / exposed	1 / 163 (0.61%)	1 / 81 (1.23%)	
occurrences (all)	1	1	
Papule			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	2 / 163 (1.23%)	1 / 81 (1.23%)	
occurrences (all)	2	1	
Pruritus generalised			
subjects affected / exposed	1 / 163 (0.61%)	1 / 81 (1.23%)	
occurrences (all)	1	1	
Psoriasis			

subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	1 / 163 (0.61%)	1 / 81 (1.23%)	
occurrences (all)	1	1	
Rosacea			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Seborrhoeic dermatitis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Skin mass			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Urticaria			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Vitiligo			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Haematuria			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Nephrolithiasis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Nephropathy			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Renal artery stenosis			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	2	

Renal cyst			
subjects affected / exposed	3 / 163 (1.84%)	1 / 81 (1.23%)	
occurrences (all)	3	1	
Renal injury			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Urinary bladder polyp			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Urinary retention			
subjects affected / exposed	1 / 163 (0.61%)	1 / 81 (1.23%)	
occurrences (all)	1	1	
Endocrine disorders			
Goitre			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Hypothyroidism			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	10 / 163 (6.13%)	8 / 81 (9.88%)	
occurrences (all)	13	9	
Arthritis			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Back pain			
subjects affected / exposed	15 / 163 (9.20%)	4 / 81 (4.94%)	
occurrences (all)	15	4	
Bone pain			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Bursa disorder			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Intervertebral disc degeneration			

subjects affected / exposed	2 / 163 (1.23%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Intervertebral disc disorder			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Limb discomfort			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
subjects affected / exposed	3 / 163 (1.84%)	5 / 81 (6.17%)	
occurrences (all)	3	7	
Muscular weakness			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal pain			
subjects affected / exposed	5 / 163 (3.07%)	0 / 81 (0.00%)	
occurrences (all)	7	0	
Myalgia			
subjects affected / exposed	4 / 163 (2.45%)	5 / 81 (6.17%)	
occurrences (all)	6	5	
Osteitis deformans			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Osteoarthritis			
subjects affected / exposed	8 / 163 (4.91%)	2 / 81 (2.47%)	
occurrences (all)	8	2	
Pain in extremity			
subjects affected / exposed	6 / 163 (3.68%)	2 / 81 (2.47%)	
occurrences (all)	7	2	
Periarthritis			
subjects affected / exposed	2 / 163 (1.23%)	0 / 81 (0.00%)	
occurrences (all)	3	0	
Rheumatoid arthritis			

subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Rib deformity			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Spinal osteoarthritis			
subjects affected / exposed	1 / 163 (0.61%)	2 / 81 (2.47%)	
occurrences (all)	2	2	
Spinal pain			
subjects affected / exposed	2 / 163 (1.23%)	1 / 81 (1.23%)	
occurrences (all)	2	1	
Trigger finger			
subjects affected / exposed	2 / 163 (1.23%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Bronchitis			
subjects affected / exposed	3 / 163 (1.84%)	3 / 81 (3.70%)	
occurrences (all)	3	3	
Bronchitis viral			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Cellulitis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Conjunctivitis			
subjects affected / exposed	2 / 163 (1.23%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Fungal infection			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Furuncle			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	

Gastroenteritis			
subjects affected / exposed	3 / 163 (1.84%)	2 / 81 (2.47%)	
occurrences (all)	4	4	
Gastroenteritis viral			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Herpes zoster			
subjects affected / exposed	2 / 163 (1.23%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Influenza			
subjects affected / exposed	4 / 163 (2.45%)	0 / 81 (0.00%)	
occurrences (all)	4	0	
Laryngitis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Localised infection			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Lower respiratory tract infection			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	35 / 163 (21.47%)	22 / 81 (27.16%)	
occurrences (all)	45	23	
Onychomycosis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Oral fungal infection			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Otitis externa			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Otitis externa bacterial			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	

Otitis media			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Paronychia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Periodontitis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Pharyngitis			
subjects affected / exposed	4 / 163 (2.45%)	1 / 81 (1.23%)	
occurrences (all)	4	1	
Pharyngitis streptococcal			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Pulpitis dental			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Pneumonia			
subjects affected / exposed	4 / 163 (2.45%)	0 / 81 (0.00%)	
occurrences (all)	4	0	
Respiratory tract infection viral			
subjects affected / exposed	0 / 163 (0.00%)	2 / 81 (2.47%)	
occurrences (all)	0	2	
Respiratory tract infection			
subjects affected / exposed	2 / 163 (1.23%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Rhinitis			
subjects affected / exposed	1 / 163 (0.61%)	2 / 81 (2.47%)	
occurrences (all)	1	2	
Sinusitis			
subjects affected / exposed	2 / 163 (1.23%)	0 / 81 (0.00%)	
occurrences (all)	3	0	
Tonsillitis			
subjects affected / exposed	0 / 163 (0.00%)	2 / 81 (2.47%)	
occurrences (all)	0	2	

Tooth abscess			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Tooth infection			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	5 / 163 (3.07%)	4 / 81 (4.94%)	
occurrences (all)	5	4	
Upper respiratory tract infection bacterial			
subjects affected / exposed	1 / 163 (0.61%)	3 / 81 (3.70%)	
occurrences (all)	2	4	
Urinary tract infection			
subjects affected / exposed	1 / 163 (0.61%)	2 / 81 (2.47%)	
occurrences (all)	1	2	
Viral infection			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Viral rhinitis			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 163 (0.61%)	1 / 81 (1.23%)	
occurrences (all)	1	1	
Wound infection			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Wound infection staphylococcal			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Diabetes mellitus inadequate control			

subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Dyslipidaemia			
subjects affected / exposed	2 / 163 (1.23%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Glucose tolerance impaired			
subjects affected / exposed	1 / 163 (0.61%)	1 / 81 (1.23%)	
occurrences (all)	1	1	
Gout			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	2	
Hypercholesterolaemia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Hyperglycaemia			
subjects affected / exposed	2 / 163 (1.23%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Hypermagnesaemia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Hypomagnesaemia			
subjects affected / exposed	0 / 163 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 163 (0.61%)	1 / 81 (1.23%)	
occurrences (all)	1	1	
Vitamin B12 deficiency			
subjects affected / exposed	1 / 163 (0.61%)	0 / 81 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 July 2014	- Inclusion criteria: Number 103: added assessment by the central imaging vendor at screening for BMD T-scores - Exclusion criteria and Excluded treatments: deleted tibolone. - Study procedures: Clarified intervals for DXA scans taken for the screening period; defined day 1 and subsequent visit dates.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported