Clinical trial results:
A Phase III Randomized, Placebo-Controlled Clinical Trial to Assess the Safety and Efficacy of Odanacatib (MK-0822) to reduce the Risk of Fracture in Osteoporotic Men Treated with Vitamin D and Calcium

Summary

EudraCT number	2010-019454-41
Trial protocol	LV DK GB NL EE IT BG
Global end of trial date	22 July 2013

Results information

Result version number	v2 (current)
This version publication date	02 July 2016
First version publication date	15 July 2015
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	0822-053

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01120600
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.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	22 July 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 July 2013
Global end of trial reached?	Yes
Global end of trial date	22 July 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1. To assess the effect in men with osteoporosis of odanacatib 50 mg once weekly versus placebo on lumbar spine bone mineral density (BMD) over 24 months; 2. To assess the safety and tolerability of odanacatib 50 mg once weekly compared to placebo.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy:

Calcium and Vitamin D3

Evidence for comparator: -

Actual start date of recruitment	09 June 2010
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	Colombia: 20
Country: Number of subjects enrolled	Chile: 2
Country: Number of subjects enrolled	United States: 61
Country: Number of subjects enrolled	Russian Federation: 20
Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	United Kingdom: 59
Country: Number of subjects enrolled	Denmark: 43
Country: Number of subjects enrolled	Estonia: 9
Country: Number of subjects enrolled	France: 16
Country: Number of subjects enrolled	Italy: 17
Country: Number of subjects enrolled	Latvia: 11
Country: Number of subjects enrolled	Japan: 24
Country: Number of subjects enrolled	Mexico: 6
Worldwide total number of subjects	294
EEA total number of subjects	161

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)	77
From 65 to 84 years	210
85 years and over	7

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were men between 40 and 95 years of age, with idiopathic osteoporosis or osteoporosis due to hypogonadism. Additional inclusion and exclusion criteria applied.

Period 1

Period 1 title	Period 1 (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	Odanacatib 50 mg once weekly

Arm description:

Participants received one Odanacatib 50 mg tablet once weekly. In addition, they received a weekly dose 5600 IU of open-label Vitamin D3 as well as a sufficient supply of open-label calcium carbonate so that their total daily calcium intake from both dietary and supplemental sources was approximately 1200 mg.

Arm type	Experimental
Investigational medicinal product name	Odanacatib
Investigational medicinal product code	
Other name	MK-0822
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Odanacatib, 50 mg tablet, once weekly

Arm title	Placebo once weekly

Arm description:

Participants received one Placebo tablet once weekly. In addition, they received a weekly dose 5600 IU of open-label Vitamin D3 as well as a sufficient supply of open-label calcium carbonate so that their total daily calcium intake from both dietary and supplemental sources was approximately 1200 mg.

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

Dosage and administration details:

Participants received one placebo to Odanacatib tablet once weekly.

Number of subjects in period 1	Odanacatib 50 mg once weekly	Placebo once weekly
Started	147	147
Treated	146	146
Completed	128	115
Not completed	19	32
Adverse event, serious fatal	2	1
Physician decision	1	3
Consent withdrawn by subject	10	11
Adverse event, non-fatal	5	6
Excessive bone loss	-	4
Lost to follow-up	1	3
Protocol deviation	-	4

Baseline characteristics

Reporting groups	
Reporting group title	Odanacatib 50 mg once weekly
Reporting group description:	
Participants received one Odanacatib 50 mg tablet once weekly. In addition, they received a weekly dose 5600 IU of open-label Vitamin D3 as well as a sufficient supply of open-label calcium carbonate so that their total daily calcium intake from both dietary and supplemental sources was approximately 1200 mg.	
Reporting group title	Placebo once weekly
Reporting group description:	
Participants received one Placebo tablet once weekly. In addition, they received a weekly dose 5600 IU of open-label Vitamin D3 as well as a sufficient supply of open-label calcium carbonate so that their total daily calcium intake from both dietary and supplemental sources was approximately 1200 mg.	

Reporting group values	Odanacatib 50 mg once weekly	Placebo once weekly	Total
Number of subjects	147	147	294
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	40	37	77
From 65-84 years	103	107	210
85 years and over	4	3	7
Age continuous Units: years			
arithmetic mean	68.9	68.7	
standard deviation	± 8.2	± 7.7	-
Gender categorical Units: Subjects			
Female	0	0	0
Male	147	147	294

End points

End points reporting groups

Reporting group title	Odanacatib 50 mg once weekly

Reporting group description:

Participants received one Odanacatib 50 mg tablet once weekly. In addition, they received a weekly dose 5600 IU of open-label Vitamin D3 as well as a sufficient supply of open-label calcium carbonate so that their total daily calcium intake from both dietary and supplemental sources was approximately 1200 mg.

Reporting group title	Placebo once weekly

Reporting group description:

Participants received one Placebo tablet once weekly. In addition, they received a weekly dose 5600 IU of open-label Vitamin D3 as well as a sufficient supply of open-label calcium carbonate so that their total daily calcium intake from both dietary and supplemental sources was approximately 1200 mg.

Primary: Percentage Change from Baseline in Lumbar Spine Bone Mineral Density at Month 24

End point title	Percentage Change from Baseline in Lumbar Spine Bone Mineral Density at Month 24

End point description:

Lumbar spine BMD was assessed by dual energy X-ray absorptiometry (DXA) at Baseline and at Months 3, 6, 12, and 24. This endpoint was based on the full analysis set (FAS) population, which consisted of all randomized participants who took at least one dose of blinded study treatment. Participants without a baseline measurement for the endpoint were excluded.

End point type	Primary

End point timeframe:

Baseline and Months 3, 6, 12, and 24

End point values	Odanacatib 50 mg once weekly	Placebo once weekly		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	107		
Units: percent change				
least squares mean (confidence interval 95%)	6.86 (6.08 to 7.64)	1.27 (0.48 to 2.06)		

Statistical analyses

Statistical analysis title	Pct Change in Lumbar Spine BMD at Month 24

Statistical analysis description:

A constrained full likelihood longitudinal data analysis (cLDA) method was used for this statistical analysis. The cLDA model included the baseline measurement and all post-baseline percent changes from baseline in the response vector, with fixed effects for treatment, time, geographic region, machine type and treatment-by-time interaction, geographic region-by-time interaction, and machine type–by-time interaction.

Comparison groups	Odanacatib 50 mg once weekly v Placebo once weekly

Number of subjects included in analysis	219
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	cLDA
Parameter estimate	Difference in LS means
Point estimate	5.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.48
upper limit	6.7

Secondary: Percentage Change from Baseline in Total Hip BMD at Month 24

End point title	Percentage Change from Baseline in Total Hip BMD at Month 24

End point description:

Total hip BMD was assessed by DXA at Baseline at Months 3, 6, 12, and 24. This endpoint was based on the FAS population, which consisted of all randomized participants who took at least one dose of blinded study treatment. Participants without a baseline measurement for the endpoint were excluded.

End point type	Secondary

End point timeframe:

Baseline and Months 3, 6, 12, and 24

End point values	Odanacatib 50 mg once weekly	Placebo once weekly		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	105		
Units: percent change				
least squares mean (confidence interval 95%)	1.91 (1.38 to 2.43)	-0.11 (-0.65 to 0.42)		

Statistical analyses

Statistical analysis title	Pct Chg from Baseline in Total Hip BMD at Month 24

Statistical analysis description:

A cLDA method was used for this statistical analysis. The cLDA model included the baseline measurement and all post-baseline percent changes from baseline in the response vector, with fixed effects for treatment, time, geographic region, machine type and treatment-by-time interaction, geographic region-by-time interaction, and machine type-by-time interaction.

Comparison groups	Odanacatib 50 mg once weekly v Placebo once weekly

Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	cLDA
Parameter estimate	Difference in LS Means
Point estimate	2.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.27
upper limit	2.77

Secondary: Percentage Change from Baseline in Femoral Neck BMD at Month 24

End point title	Percentage Change from Baseline in Femoral Neck BMD at Month 24

End point description:

Fermoral neck BMD was assessed by DXA at Baseline and at Months 3, 6, 12, and 24. This endpoint was based on the FAS population, which consisted of all randomized participants who took at least one dose of blinded study treatment. Participants without a baseline measurement for the endpoint were excluded.

End point type	Secondary

End point timeframe:

Baseline and Months 3, 6, 12, and 24

End point values	Odanacatib 50 mg once weekly	Placebo once weekly		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	105		
Units: percent change				
least squares mean (confidence interval 95%)	1.69 (0.82 to 2.55)	0 (-0.89 to 0.88)		

Statistical analyses

Statistical analysis title	Pct Chg from Baseline in Fem Neck BMD at Month 24

Statistical analysis description:

A cLDA method was used for this statistical analysis. The cLDA model included the baseline measurement and all post-baseline percent changes from baseline in the response vector, with fixed effects for treatment, time, geographic region, machine type and treatment-by-time interaction, geographic region-by-time interaction, and machine type–by-time interaction.

Comparison groups	Odanacatib 50 mg once weekly v Placebo once weekly

Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.008
Method	cLDA
Parameter estimate	Difference in LS Means
Point estimate	1.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.45
upper limit	2.93

Secondary: Percentage Change from Baseline in Trochanter BMD at Month 24

End point title	Percentage Change from Baseline in Trochanter BMD at Month 24

End point description:

Trochanter BMD was assessed by DXA at Baseline and at Months 3, 6, 12, and 24. This endpoint was based on the FAS population, which consisted of all randomized participants who took at least one dose of blinded study treatment. Participants without a baseline measurement for the endpoint were excluded.

End point type	Secondary

End point timeframe:

Baseline and Months 3, 6, 12, and 24

End point values	Odanacatib 50 mg once weekly	Placebo once weekly		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	105		
Units: percent change				
least squares mean (confidence interval 95%)	2.77 (1.94 to 3.6)	0.66 (-0.18 to 1.5)		

Statistical analyses

Statistical analysis title	Pct Chg from Baseline in Trochanter BMD at Mo 24

Statistical analysis description:

A cLDA method was used for this statistical analysis. The cLDA model included the baseline measurement and all post-baseline percent changes from baseline in the response vector, with fixed effects for treatment, time, geographic region, machine type and treatment-by-time interaction, geographic region-by-time interaction, and machine type-by-time interaction.

Comparison groups	Odanacatib 50 mg once weekly v Placebo once weekly

Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	cLDA
Parameter estimate	Difference in LS Means
Point estimate	2.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	3.3

Secondary: Percentage Change from Baseline in Serum C-Telopeptides of Type 1 Collagen (s-CTx) at Month 24

End point title	Percentage Change from Baseline in Serum C-Telopeptides of Type 1 Collagen (s-CTx) at Month 24

End point description:

Serum samples were collected to evaluate biochemical markers for s-CTx, which were measured at Baseline and at Months 3, 6, 12, 18, and 24. This endpoint was based on the Per-Protocol (PP) population, which excluded participants due to important deviations from the protocol that may have substantially affected the results.

End point type	Secondary

End point timeframe:

Baseline and Months 3, 6, 12, 18, and 24

End point values	Odanacatib 50 mg once weekly	Placebo once weekly		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	102		
Units: percent change				
least squares mean (confidence interval 95%)	-20.07 (-28.36 to -10.82)	56.51 (40.01 to 74.96)		

Statistical analyses

Statistical analysis title	Pct Change from Baseline in s-CTx at Month 24

Statistical analysis description:

A cLDA method was used for this statistical analysis. The cLDA model includes the log-transformed baseline and log-transformed post-baseline measurements up to Month 24 in the response vector, with fixed effects for treatment, time, geographic region, treatment-by-time interaction and geographic region-by-time interaction.

Comparison groups	Odanacatib 50 mg once weekly v Placebo once weekly

Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	cLDA
Parameter estimate	Difference in LS Means
Point estimate	-76.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-92.56
upper limit	-60.61

Secondary: Percentage Change from Baseline in Urine Collagen N-Telopeptide/Creatinine Ratio (U-NTx/Cr) at Month 24

End point title	Percentage Change from Baseline in Urine Collagen N-Telopeptide/Creatinine Ratio (U-NTx/Cr) at Month 24

End point description:

Urine samples were collected to evaluate biochemical markers for u-NTx/Cr, which were measured at Baseline and at Months 3, 6, 12, 18, and 24. This endpoint was based on the Per-Protocol (PP) population, which excluded participants due to important deviations from the protocol that may have substantially affected the results.

End point type	Secondary

End point timeframe:

Baseline and Months 3, 6, 12, 18, and 24

End point values	Odanacatib 50 mg once weekly	Placebo once weekly		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	102		
Units: percent change				
least squares mean (confidence interval 95%)	-61.43 (-64.71 to -57.85)	6.65 (-2.68 to 16.87)		

Statistical analyses

Statistical analysis title	Pct Change from Baseline in u-NTx/Cr at Month 24

Statistical analysis description:

A cLDA method was used for this statistical analysis. The cLDA model includes the log-transformed baseline and log-transformed post-baseline measurements up to Month 24 in the response vector, with fixed effects for treatment, time, geographic region, treatment-by-time interaction and geographic region-by-time interaction.

Comparison groups	Odanacatib 50 mg once weekly v Placebo once weekly

Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	cLDA
Parameter estimate	Difference in LS Means
Point estimate	-68.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-78.1
upper limit	-58.06

Secondary: Percentage Change from Baseline in Serum Bone-Specific Alkaline Phosphatase (s-BSAP) at Month 24

End point title	Percentage Change from Baseline in Serum Bone-Specific Alkaline Phosphatase (s-BSAP) at Month 24

End point description:

Biochemical markers for s-BSAP were measured at Baseline and at Months 3, 6, 12, 18, and 24. This endpoint was based on the Per-Protocol (PP) population, which excluded participants due to important deviations from the protocol that may have substantially affected the results.

End point type	Secondary

End point timeframe:

Months 3, 6, 12, 18, and 24

End point values	Odanacatib 50 mg once weekly	Placebo once weekly		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	114	110		
Units: percent change				
least squares mean (confidence interval 95%)	-5.28 (-9.76 to -0.57)	2.66 (-2.25 to 7.82)		

Statistical analyses

Statistical analysis title	Pct Change From Baseline in s-BSAP at Month 24

Statistical analysis description:

A cLDA method was used for this statistical analysis. The cLDA model includes the log-transformed baseline and log-transformed post-baseline measurements up to Month 24 in the response vector, with fixed effects for treatment, time, geographic region, treatment-by-time interaction and geographic region-by-time interaction.

Comparison groups	Odanacatib 50 mg once weekly v Placebo once weekly

Number of subjects included in analysis	224
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.019
Method	cLDA
Parameter estimate	Difference in LS Means
Point estimate	-7.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.58
upper limit	-1.31

Secondary: Percentage Change from Baseline in Serum N-Terminal Propeptides of Type I Collagen (s-P1NP) at Month 24

End point title	Percentage Change from Baseline in Serum N-Terminal Propeptides of Type I Collagen (s-P1NP) at Month 24

End point description:

Serum samples were collected to evaluated biochemical markers for s-P1NP, which were measured at Baseline and at Months 3, 6, 12, 18, and 24. This endpoint was based on the Per-Protocol (PP) population, which excluded participants due to important deviations from the protocol that may have substantially affected the results.

End point type	Secondary

End point timeframe:

Baseline and Months 3, 6, 12, 18, and 24

End point values	Odanacatib 50 mg once weekly	Placebo once weekly		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	114	110		
Units: percent change				
least squares mean (confidence interval 95%)	-10.94 (-17.27 to -4.14)	5.06 (-2.47 to 13.17)		

Statistical analyses

Statistical analysis title	Pct Change from Baseline in s-P1NP at Month 24

Statistical analysis description:

A cLDA method was used for this statistical analysis. The cLDA model includes the log-transformed baseline and log-transformed post-baseline measurements up to Month 24 in the response vector, with fixed effects for treatment, time, geographic region, treatment-by-time interaction and geographic region-by-time interaction.

Comparison groups	Odanacatib 50 mg once weekly v Placebo once weekly

Number of subjects included in analysis	224
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001
Method	cLDA
Parameter estimate	Difference in LS Means
Point estimate	-16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.74
upper limit	-6.27

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 24 Months after first dose of study drug

Adverse event reporting additional description:

Safety analyses were performed using the All-Patients-as-Treated (APaT) population, which included all participants who took at least one dose of study medication.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Placebo once weekly

Reporting group description: -

Reporting group title	Odanacatib 50 mg once weekly

Reporting group description: -

Serious adverse events	Placebo once weekly	Odanacatib 50 mg once weekly	
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 146 (17.81%)	26 / 146 (17.81%)	
number of deaths (all causes)	2	2	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign gastric neoplasm			
subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial carcinoma			

subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic lymphocytic leukaemia			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemangioma of bone			
subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-Hodgkin's lymphoma			
subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Prostate cancer			
subjects affected / exposed	2 / 146 (1.37%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cell carcinoma			

subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell lung cancer			
subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Multi-organ failure			
subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			

subjects affected / exposed	0 / 146 (0.00%)	2 / 146 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Weight decreased			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (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			
Clavicle fracture			
subjects affected / exposed	1 / 146 (0.68%)	2 / 146 (1.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fractured sacrum			
subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heat exhaustion			

subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ilium fracture			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative hernia			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (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 / 146 (0.68%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Hydrocele			

subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			
subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	2 / 146 (1.37%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			

subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sick sinus syndrome			
subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral ischaemia			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (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	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic infarction			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Inguinal hernia			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Mallory-Weiss syndrome			
subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Alcoholic liver disease			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cholecystitis acute			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis obstructive			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Calculus ureteric			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			

subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemarthrosis			
subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 146 (0.00%)	2 / 146 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myopathy			
subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	1 / 146 (0.68%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendonitis			
subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis infective			
subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			

subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 146 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (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	1 / 146 (0.68%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal infection			
subjects affected / exposed	1 / 146 (0.68%)	0 / 146 (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: 5 %

Non-serious adverse events	Placebo once weekly	Odanacatib 50 mg once weekly	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 146 (30.14%)	30 / 146 (20.55%)	
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	9 / 146 (6.16%)	4 / 146 (2.74%)	
occurrences (all)	11	4	
Musculoskeletal and connective tissue			

disorders			
Arthralgia			
subjects affected / exposed	10 / 146 (6.85%)	4 / 146 (2.74%)	
occurrences (all)	11	4	
Back pain			
subjects affected / exposed	12 / 146 (8.22%)	9 / 146 (6.16%)	
occurrences (all)	15	11	
Pain in extremity			
subjects affected / exposed	10 / 146 (6.85%)	3 / 146 (2.05%)	
occurrences (all)	12	3	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	15 / 146 (10.27%)	14 / 146 (9.59%)	
occurrences (all)	18	18	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported