Clinical trial results:
An Imaging Sub-Study of the Phase 3 Randomized, Placebo-Controlled Clinical Trial to Assess the Safety and Efficacy of Odanacatib (MK-0822) to Reduce the Risk of Fracture in Osteoporotic Postmenopausal Women Treated With Vitamin D and Calcium

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2008-004578-42
Trial protocol	DK CZ EE
Global end of trial date	11 November 2014

Results information

Result version number	v1 (current)
This version publication date	15 May 2016
First version publication date	15 May 2016

Trial information

Trial identification

Sponsor protocol code	MK-0822-032

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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	11 November 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 November 2012
Global end of trial reached?	Yes
Global end of trial date	11 November 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This was an Imaging Sub-Study of Protocol MK-0822-018, A Study of MK-0822 in Postmenopausal Women With Osteoporosis to Assess Fracture Risk. Study MK-0822-018 was an event-driven trial to determine the safety and efficacy, especially fracture-risk reduction, of odanacatib in postmenopausal women 65 years and older who have been diagnosed with osteoporosis.

The main objective of this Imaging Sub-Study (MK-0822-032) was to evaluate the effect of treatment with MK-0822 50 mg once weekly on percent change from baseline in trabecular volumetric bone mineral density (vBMD) at the lumbar spine, compared to placebo at Month 24. The percent change was assessed using Quantitative Computed Tomography (QCT). The primary hypothesis was as follows: Compared to placebo, MK-0822 will increase trabecular vBMD at the lumbar spine (assessed by QCT) from baseline at Month 24.

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:

Treatment of postmenopausal women with osteoporosis

Evidence for comparator: -

Actual start date of recruitment	02 February 2009
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	Denmark: 103
Country: Number of subjects enrolled	South Africa: 61
Worldwide total number of subjects	164
EEA total number of subjects	103

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)	0
From 65 to 84 years	160
85 years and over	4

Subject disposition

Recruitment

Recruitment details:

This Sub-Study enrolled postmenopausal women with osteoporosis from Study MK-0822-018. Other inclusion and exclusion criteria applied.

Pre-assignment

Screening details:

A total of 164 participants from Study MK-0822-018 were enrolled in Sub-Study MK-0822-032. Of those enrolled, 160 participants received treatment and were included in the All-Patients-Treated population.

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	Odanacatib 50 mg once weekly

Arm description:

Participants received 50 mg of blinded odanacatib once weekly over the course of Study MK-0822-018 and the first Extension (5 years total). Participants also received Vitamin D3 and open-label supplemental calcium so that 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:

50 mg of odanacatib once weekly over the course of the Base study and first Extension

Arm title	Placebo once weekly

Arm description:

Participants received placebo to odanacatib 50 mg weekly over the course of Study MK-0822-018 and the first Extension. Participants also received Vitamin D3 and open-label supplemental calcium so that 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:

50 mg placebo tablet to odanacatib once weekly over the course of the Base study and first Extension

Number of subjects in period 1	Odanacatib 50 mg once weekly	Placebo once weekly
Started	78	86
Completed	57	61
Not completed	21	25
Withdrawal By Subject	3	8
Adverse event, non-fatal	11	7
Other Protocol Specified Criteria	6	9
Protocol deviation	1	-
Lack of efficacy	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Odanacatib 50 mg once weekly
Reporting group description:	
Participants received 50 mg of blinded odanacatib once weekly over the course of Study MK-0822-018 and the first Extension (5 years total). Participants also received Vitamin D3 and open-label supplemental calcium so that 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 placebo to odanacatib 50 mg weekly over the course of Study MK-0822-018 and the first Extension. Participants also received Vitamin D3 and open-label supplemental calcium so that 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	78	86	164
Age Categorical			
Units: Subjects			
Age Continuous			
Units: years			
arithmetic mean	71.3	72.9	
standard deviation	± 5.7	± 5.7	-
Gender Categorical			
Units: Subjects			
Female	78	86	164
Male	0	0	0

End points

End points reporting groups

Reporting group title	Odanacatib 50 mg once weekly

Reporting group description:

Participants received 50 mg of blinded odanacatib once weekly over the course of Study MK-0822-018 and the first Extension (5 years total). Participants also received Vitamin D3 and open-label supplemental calcium so that 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 placebo to odanacatib 50 mg weekly over the course of Study MK-0822-018 and the first Extension. Participants also received Vitamin D3 and open-label supplemental calcium so that total daily calcium intake (from both dietary and supplemental sources) was approximately 1200 mg.

Primary: Percent Change From Baseline in Spine (L1) Trabecular vBMD at Total Vertebral Body (mg/cm3) at Month 24

End point title	Percent Change From Baseline in Spine (L1) Trabecular vBMD at Total Vertebral Body (mg/cm3) at Month 24

End point description:

Trabecular vBMD of the lumbar spine was assessed using QCT at Baseline and at Months 12, 24, and 36. This endpoint was based on the full analysis set (FAS) population, which consisted of all randomized participants who received at least one dose of blinded study treatment, have a baseline measurement andat least one on-treatment measurement available.

End point type	Primary

End point timeframe:

Baseline to Month 24

End point values	Odanacatib 50 mg once weekly	Placebo once weekly		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	48		
Units: Percent change				
least squares mean (confidence interval 95%)	8.05 (4.48 to 11.62)	-0.87 (-4.37 to 2.64)		

Statistical analyses

Statistical analysis title	Difference in Least Squares Means

Statistical analysis description:

A longitudinal data analysis (LDA) model that included time points at Months 12, 24, and 36, and also factors for treatment, stratum (prior vertebral fracture [yes/no]) and the interaction of time by treatment, was used.

Comparison groups	Placebo once weekly v Odanacatib 50 mg once weekly

Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	LDA model
Parameter estimate	Difference in LS Means
Point estimate	8.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.9
upper limit	13.93

Secondary: Percent Change From Baseline in QCT Total Hip Cortical vBMD (mg/cm3) at Month 24

End point title	Percent Change From Baseline in QCT Total Hip Cortical vBMD (mg/cm3) at Month 24

End point description:

Cortical vBMD of the hip was assessed using QCT at Baseline and at Months 12, 24, and 36. This endpoint was based on the full analysis set (FAS) population, which consisted of all randomized participants who received at least one dose of blinded study treatment, have a baseline measurement and at least one on-treatment measurement available.

End point type	Secondary

End point timeframe:

Baseline to Month 24

End point values	Odanacatib 50 mg once weekly	Placebo once weekly		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	55		
Units: Percent change				
least squares mean (confidence interval 95%)	3.29 (2.33 to 4.24)	0.52 (-0.39 to 1.44)		

Statistical analyses

Statistical analysis title	Difference in Least Squares Means

Statistical analysis description:

LDA method that included time points at Months 12, 24, and 36 was used for analysis of QCT Total Hip Cortical vBMD.

Comparison groups	Odanacatib 50 mg once weekly v Placebo once weekly

Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	LDA model
Parameter estimate	Difference in LS Means
Point estimate	2.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.43
upper limit	4.1

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

With the exception of the qualitative assessment of transilial bone biopsies, there were no safety assessments planned in the context of Sub-Study MK-0822-032. Participant safety assessments will be contained within Study MK-0822-018.

Assessment type	Non-systematic

Dictionary used

Dictionary name	Not applicable
Dictionary version	N/A

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: With the exception of the qualitative assessment of transilial bone biopsies, there were no safety assessments planned in the context of Sub-Study MK-0822-032. Participant safety assessments will be contained within Study MK-0822-018.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 June 2009	Amendment 1: The primary reasons for this amendment were as follows: new information based on Denmark MSD site allocation of participants for Protocol 018; incorporated suggestions and requirements from regulatory agencies and ethics review committee during the protocol review and approval process for the "Lead Cohort"; and clarified protocol based on questions received from sites.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported