Clinical trial results:
A 1-Year, Worldwide, Multicenter, Double-Blind, Randomized, Parallel, Placebo-Controlled Study to Assess the Efficacy and Tolerability of Anacetrapib When Added to Ongoing Statin Therapy With or Without Other Lipid Modifying Medication(s) in Patients with Heterozygous Familial Hypercholesterolemia (REALIZE)

Summary

EudraCT number	2011-004525-27
Trial protocol	GB DE NL ES CZ
Global end of trial date	

Results information

Result version number	v1
This version publication date	05 April 2016
First version publication date	19 July 2015

Trial information

Trial identification

Sponsor protocol code	MK-0859-020

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01524289
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	Interim
Date of interim/final analysis	12 February 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 February 2014
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

1. Evaluate the efficacy of adding anacetrapib 100 mg for 52 weeks relative to placebo on plasma concentrations of low-density lipoprotein-cholesterol (LDL-C).
2. Evaluate the safety and tolerability of 52 weeks of treatment with anacetrapib 100 mg.

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:

Participants were treated with an optimal dose of statin, (i.e. doses of statin >= simvastatin 40 mg, atorvastatin 20 mg, rosuvastatin 5 mg, pitavastatin 4 mg, lovastatin 80 mg or pravastatin 80 mg), ± other lipid-modifying medication(s) for at least 6 weeks prior to Visit 1.

Evidence for comparator: -

Actual start date of recruitment	03 February 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 102
Country: Number of subjects enrolled	Norway: 29
Country: Number of subjects enrolled	Spain: 48
Country: Number of subjects enrolled	United Kingdom: 25
Country: Number of subjects enrolled	France: 20
Country: Number of subjects enrolled	Germany: 15
Country: Number of subjects enrolled	Canada: 50
Country: Number of subjects enrolled	Russian Federation: 8
Country: Number of subjects enrolled	United States: 9
Worldwide total number of subjects	306
EEA total number of subjects	239

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)	239
From 65 to 84 years	67
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were to complete a 2-week placebo run-in, a 52-week treament period and a 12-week reversal period (safety follow-up).

Pre-assignment

Screening details:

The study enrolled participants 18 to 80 years of age, with a genotype-confirmed or clinical diagnosis of heterozygous familial hypercholesterolemia (HeFH) and had been treated with an optimal dose of statin for at least 6 weeks. Other inclusion and exclusion criteria applied.

Period 1

Period 1 title	Treatment 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	Anacetrapib 100 mg

Arm description:

One tablet of anacetrapib 100 mg once daily with a meal for 52 weeks

Arm type	Experimental
Investigational medicinal product name	Anacetrapib
Investigational medicinal product code	
Other name	MK-0859
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One 100 mg tablet once daily for 52 weeks

Arm title	Placebo

Arm description:

One matching placebo tablet once daily with a meal for 52 weeks

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

Dosage and administration details:

one placebo tablet once daily for 52 weeks

Number of subjects in period 1	Anacetrapib 100 mg	Placebo
Started	204	102
Treated	203	102
Completed	174	88
Not completed	30	14
Physician decision	1	-
Consent withdrawn by subject	11	7
Adverse event, non-fatal	12	5
did not take study medication	1	-
Lost to follow-up	-	1
Protocol deviation	5	1

Period 2

Period 2 title	Reversal Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Anacetrapib 100 mg - Reversal

Arm description:

Participants who completed treatment period and participants who were discontinued during treatment period (non-completers) who were administered anacetrapib in treatment period and entered reversal period. No study drug was administered during Reversal Period.

Arm type	Experimental
Investigational medicinal product name	Anacetrapib
Investigational medicinal product code	
Other name	MK-0859
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One 100 mg tablet once daily for 52 weeks

Arm title	Placebo - Reversal

Arm description:

Participants who completed treatment period and participants who were discontinued during treatment period (non-completers) who were administered placebo in treatment period and entered reversal period. No study drug was administered during Reversal Period.

Arm type	Placebo

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

Dosage and administration details:

One placebo tablet once daily for 52 weeks

Number of subjects in period 2	Anacetrapib 100 mg - Reversal	Placebo - Reversal
Started	174	88
Completed	195	95
Not completed	1	0
Consent withdrawn by subject	1	-
Joined	22	7
Non-completers from treatment period	22	7

Baseline characteristics

Reporting groups	
Reporting group title	Anacetrapib 100 mg
Reporting group description:	
One tablet of anacetrapib 100 mg once daily with a meal for 52 weeks	
Reporting group title	Placebo
Reporting group description:	
One matching placebo tablet once daily with a meal for 52 weeks	

Reporting group values	Anacetrapib 100 mg	Placebo	Total
Number of subjects	204	102	306
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	55	55.7	
standard deviation	± 11.8	± 11.9	-
Gender categorical Units: Subjects			
Female	84	52	136
Male	120	50	170

End points

End points reporting groups

Reporting group title	Anacetrapib 100 mg
Reporting group description:	
One tablet of anacetrapib 100 mg once daily with a meal for 52 weeks	
Reporting group title	Placebo
Reporting group description:	
One matching placebo tablet once daily with a meal for 52 weeks	
Reporting group title	Anacetrapib 100 mg - Reversal
Reporting group description:	
Participants who completed treatment period and participants who were discontinued during treatment period (non-completers) who were administered anacetrapib in treatment period and entered reversal period. No study drug was administered during Reversal Period.	
Reporting group title	Placebo - Reversal
Reporting group description:	
Participants who completed treatment period and participants who were discontinued during treatment period (non-completers) who were administered placebo in treatment period and entered reversal period. No study drug was administered during Reversal Period.	
Subject analysis set title	Anacetrapib 100 mg- Efficacy Population
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants who received at least 1 dose of study treatment had baseline data and at least 1 post-dose observation for the analysis endpoint.	
Subject analysis set title	Placebo - Efficacy Population
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants who received at least 1 dose of study treatment had baseline data and at least 1 post-dose observation for the analysis endpoint.	
Subject analysis set title	Anacetrapib 100 mg - Safety Population
Subject analysis set type	Safety analysis
Subject analysis set description:	
All particpants who receive at least 1 dose of study drug.	
Subject analysis set title	Placebo - Safety Population
Subject analysis set type	Safety analysis
Subject analysis set description:	
All participants who receive at least 1 dose of study drug.	

Primary: Percent Change From Baseline in Low-density Lipoprotein-cholesterol (LDL-C)

End point title	Percent Change From Baseline in Low-density Lipoprotein-cholesterol (LDL-C)
End point description:	
LDL-C levels measured at baseline and after 52 weeks of treatment using beta quantification method.	
End point type	Primary
End point timeframe:	
Baseline and Week 52	

End point values	Anacetrapib 100 mg- Efficacy Population	Placebo - Efficacy Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	165[1]	85[2]		
Units: Percentage change				
least squares mean (confidence interval 95%)	-36 (-39.5 to -32.5)	3.7 (-1.2 to 8.6)		

Notes:

[1] - met criteria for inclusion in analysis of endpoint

[2] - met criteria for inclusion in analysis of endpoint

Statistical analyses

Statistical analysis title	Comparison of Percent Change from Baseline

Statistical analysis description:

Between group comparison of percent change from baseline performed using Constrained Longitudinal Data Analysis (cLDA) model with terms for treatment, time, and the interaction of time by treatment. Analysis population defined as participants who receive at least 1 dose of study treatment and have baseline and at least 1 post-randomization observation for the analysis endpoint.

Comparison groups	Anacetrapib 100 mg- Efficacy Population v Placebo - Efficacy Population
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Difference in Least Squares Mean
Point estimate	-39.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-45.7
upper limit	-33.7

Primary: Percentage of Participants With Any Adverse Event (AE)-Treatment Period

End point title	Percentage of Participants With Any Adverse Event (AE)-Treatment Period

End point description:

An AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study drug, whether or not considered related to the use of the drug. Any worsening of a preexisting condition which is temporally associated with the use of the study drug is also an AE.

End point type	Primary

End point timeframe:

Up to 52 weeks

End point values	Anacetrapib 100 mg - Safety Population	Placebo - Safety Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	203	102		
Units: Percentage of Participants				
number (not applicable)	76.4	78.4		

Statistical analyses

Statistical analysis title	Difference in Percentages Between Groups
Comparison groups	Anacetrapib 100 mg - Safety Population v Placebo - Safety Population
Number of subjects included in analysis	305
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percentages
Point estimate	-2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.5
upper limit	8.4

Primary: Percentage of Participants With Any Drug-related AE - Treatment Period

End point title	Percentage of Participants With Any Drug-related AE - Treatment Period

End point description:

An AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study drug, whether or not considered related to the use of the drug. Any worsening of a preexisting condition which is temporally associated with the use of the study drug is also an AE. AEs reported by the investigator as definitely, probably or possibly related to study drug were considered drug-related.

End point type	Primary

End point timeframe:

Up to 52 weeks

End point values	Anacetrapib 100 mg - Safety Population	Placebo - Safety Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	203	102		
Units: Percentage of Participants				
number (not applicable)	18.2	13.7		

Statistical analyses

Statistical analysis title	Difference in Percentage Between Groups
Statistical analysis description:	
Difference in percentages between groups compared using Miettinen and Nurminen method	
Comparison groups	Anacetrapib 100 mg - Safety Population v Placebo - Safety Population
Number of subjects included in analysis	305
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percentages
Point estimate	4.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	12.6

Primary: Percentage of Participants With Any Serious Adverse Event (SAE) - Treatment Period

End point title	Percentage of Participants With Any Serious Adverse Event (SAE) - Treatment Period
End point description:	
An AE or suspected adverse reaction is considered an SAE if it results in any of the following outcomes: death, a life-threatening AE, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect.	
End point type	Primary
End point timeframe:	
Up to 52 weeks	

End point values	Anacetrapib 100 mg - Safety Population	Placebo - Safety Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	203	102		
Units: Percentage of Participants				
number (not applicable)	8.9	9.8		

Statistical analyses

Statistical analysis title	Difference in Percentages Between Groups
Comparison groups	Anacetrapib 100 mg - Safety Population v Placebo - Safety Population
Number of subjects included in analysis	305
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentages
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.9
upper limit	5.6

Primary: Percentage of Participants With Any Drug-related SAE - Treatment Period	
End point title	Percentage of Participants With Any Drug-related SAE - Treatment Period
End point description:	
An AE or suspected adverse reaction is considered an SAE if it results in any of the following outcomes: death, a life-threatening AE, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect. SAEs reported by the investigator as definitely, probably or possibly related to study were considered to be drug-related.	
End point type	Primary
End point timeframe:	
Up to 52 weeks	

End point values	Anacetrapib 100 mg - Safety Population	Placebo - Safety Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	203	102		
Units: Percentage of Participants				
number (not applicable)	0	0		

Statistical analyses

Statistical analysis title	Difference in Percentages Between Groups
Comparison groups	Placebo - Safety Population v Anacetrapib 100 mg - Safety Population
Number of subjects included in analysis	305
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percentages
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.6
upper limit	1.9

Primary: Percentage of Participants With Any AE Leading to Discontinuation of Treatment

End point title	Percentage of Participants With Any AE Leading to Discontinuation of Treatment

End point description:

An AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study drug, whether or not considered related to the use of the drug. Any worsening of a preexisting condition which is temporally associated with the use of the study drug is also an AE. Adverse Events that were reported as the cause for discontinuation of the study drug were recorded.

End point type	Primary

End point timeframe:

Up to 52 weeks

End point values	Anacetrapib 100 mg - Safety Population	Placebo - Safety Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	203	102		
Units: Percentage of Participants				
number (not applicable)	5.9	4.9		

Statistical analyses

Statistical analysis title	Difference in Percentages Between Groups
Comparison groups	Anacetrapib 100 mg - Safety Population v Placebo - Safety Population

Number of subjects included in analysis	305
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percentages
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.5
upper limit	6.1

Primary: Percentage of Participants With Elevations in Systolic Blood Pressure (SBP) >= 10 mm Hg

End point title	Percentage of Participants With Elevations in Systolic Blood Pressure (SBP) >= 10 mm Hg

End point description:

Participants had SBP assessed at baseline and throughout the 52 week treatment period. Participants who had a SBP reading that was >= 10 mm Hg higher than their baseline SBP for any assessment performed during the treatment period were recorded.

End point type	Primary

End point timeframe:

Up to 52 weeks

End point values	Anacetrapib 100 mg - Safety Population	Placebo - Safety Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	202	101		
Units: Percentage of Participants				
number (not applicable)	45	53.5		

Statistical analyses

Statistical analysis title	Difference in Percentages Between Groups
Comparison groups	Placebo - Safety Population v Anacetrapib 100 mg - Safety Population
Number of subjects included in analysis	303
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.168
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percentages
Point estimate	-8.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.1
upper limit	3.5

Primary: Percentage of Participants With Elevations in SBP >= 15 mm Hg

End point title	Percentage of Participants With Elevations in SBP >= 15 mm Hg

End point description:

Participants had SBP assessed at baseline and throughout the 52 week treatment period. Participants who had a SBP reading that was >= 15 mm Hg higher than their baseline SBP for any assessment performed during the treatment period were recorded.

End point type	Primary

End point timeframe:

Up to 52 weeks

End point values	Anacetrapib 100 mg - Safety Population	Placebo - Safety Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	202	101		
Units: Percentage of Participants				
number (not applicable)	26.2	33.7		

Statistical analyses

Statistical analysis title	Difference in Percentages Between Groups
Comparison groups	Anacetrapib 100 mg - Safety Population v Placebo - Safety Population
Number of subjects included in analysis	303
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.179
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percentages
Point estimate	-7.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.7
upper limit	3.3

Primary: Percentage of Participants With Elevations in Diastolic Blood Pressure (DBP) >= 10 mm Hg

End point title	Percentage of Participants With Elevations in Diastolic Blood Pressure (DBP) >= 10 mm Hg

End point description:

Participants had DBP assessed at baseline and throughout the 52 week treatment period. Participants who had a DBP reading that was >= 10 mm Hg higher than their baseline DBP for any assessment performed during the treatment period were recorded.

End point type	Primary

End point timeframe:

Up to 52 weeks

End point values	Anacetrapib 100 mg - Safety Population	Placebo - Safety Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	202	101		
Units: Percentage of Participants				
number (not applicable)	22.8	36.6		

Statistical analyses

Statistical analysis title	Difference in Percentages Between Group
Comparison groups	Anacetrapib 100 mg - Safety Population v Placebo - Safety Population
Number of subjects included in analysis	303
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.011
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percentages
Point estimate	-13.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25
upper limit	-3.1

Primary: Percentage of Participants With Sodium Levels > Upper limit of normal (ULN)

End point title	Percentage of Participants With Sodium Levels > Upper limit of normal (ULN)

End point description:

Participants had sodium levels assessed throughout the 52 week treatment period. Participants who had any sodium level that was > the ULN of 145 mEq/L were recorded.

End point type	Primary

End point timeframe:

Up to 52 weeks

End point values	Anacetrapib 100 mg - Safety Population	Placebo - Safety Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	202	101		
Units: Percentage of Participants				
number (not applicable)	11.4	9.9		

Statistical analyses

Statistical analysis title	Difference in Percentages Between Groups
Comparison groups	Anacetrapib 100 mg - Safety Population v Placebo - Safety Population
Number of subjects included in analysis	303
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.696
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percentages
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.8
upper limit	8.4

Primary: Percentage of Participants With Chloride Levels > ULN

End point title	Percentage of Participants With Chloride Levels > ULN

End point description:

Participants had chloride levels assessed throughout the 52 week treatment period. Participants who had any chloride level that was > the ULN of 110 mEq/L were recorded.

End point type	Primary

End point timeframe:

up to 52 weeks

End point values	Anacetrapib 100 mg - Safety Population	Placebo - Safety Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	202	101		
Units: Percentage of Participants				
number (not applicable)	0.5	0		

Statistical analyses

Statistical analysis title	Difference in Percentages Between Groups
Comparison groups	Anacetrapib 100 mg - Safety Population v Placebo - Safety Population
Number of subjects included in analysis	303
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.48
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percentages
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.2
upper limit	2.8

Primary: Percentage of Participants With Potassium Levels < Lower limit of normal (LLN)

End point title	Percentage of Participants With Potassium Levels < Lower limit of normal (LLN)

End point description:

Participants had potassium levels assessed throughout the 52 week treatment period. Participants who had any potassium level that was < the LLN of 3.5 mEq/L were recorded.

End point type	Primary

End point timeframe:

Up to 52 weeks

End point values	Anacetrapib 100 mg - Safety Population	Placebo - Safety Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	202	101		
Units: Perentage of Participants				
number (not applicable)	1.5	1		

Statistical analyses

Statistical analysis title	Difference in Percentages Between Groups
Comparison groups	Anacetrapib 100 mg - Safety Population v Placebo - Safety Population
Number of subjects included in analysis	303
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.722
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percentages
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	3.5

Primary: Percentage of Participants With Bicarbonate Levels > ULN

End point title	Percentage of Participants With Bicarbonate Levels > ULN
End point description:	
Participants had bicarbonate levels assessed throughout the 52 week treatment period. Participants who had any bicarbonate level that was > the ULN of 33 mEq/L were recorded.	
End point type	Primary
End point timeframe:	
up to 52 weeks	

End point values	Anacetrapib 100 mg - Safety Population	Placebo - Safety Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	202	101		
Units: Percentage of Participants				
number (not applicable)	0	0		

Statistical analyses

Statistical analysis title	Difference in Percentages Between Groups
Comparison groups	Anacetrapib 100 mg - Safety Population v Placebo - Safety Population
Number of subjects included in analysis	303
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percentages
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.7
upper limit	1.9

Primary: Percentage of (Participants With Consecutive Elevations in Alanine Aminotransferase ALT) and/or Aspartate Aminotransferase (AST) of >=3 x ULN

End point title	Percentage of (Participants With Consecutive Elevations in Alanine Aminotransferase ALT) and/or Aspartate Aminotransferase (AST) of >=3 x ULN

End point description:

Participants had AST and ALT levels assessed throughout the 52 week treatment period. Participants who had 2 consecutive assessments of either AST or ALT that were 3 x ULN or greater were recorded. The AST UNLs for males and females were 43 U/L and 36 U/L, respectively. The ALT UNLs for males and females were 40 U/L and 33 U/L, respectively.

End point type	Primary

End point timeframe:

Up to 52 weeks

End point values	Anacetrapib 100 mg - Safety Population	Placebo - Safety Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	202	101		
Units: Percentage of Participants				
number (not applicable)	1.5	1		

Statistical analyses

Statistical analysis title	Difference in Percentages Between Groups
Comparison groups	Anacetrapib 100 mg - Safety Population v Placebo - Safety Population

Number of subjects included in analysis	303
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.722
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percentages
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	3.5

Primary: Percentage of Participants With Creatine Kinase (CK) >=10 x ULN	
End point title	Percentage of Participants With Creatine Kinase (CK) >=10 x ULN
End point description:	
Participants had CK assessed throughout the 52 week treatment period. Participants who had any CK level that was >=10 x ULN were recorded. The UNLs for males and females were 207 U/L and 169 U/L, respectively.	
End point type	Primary
End point timeframe:	
Up to 52 weeks	

End point values	Anacetrapib 100 mg - Safety Population	Placebo - Safety Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	202	101		
Units: Percentage of Participants				
number (not applicable)	0	1		

Statistical analyses

Statistical analysis title	Difference in Percentages Between Groups
Comparison groups	Anacetrapib 100 mg - Safety Population v Placebo - Safety Population
Number of subjects included in analysis	303
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.157
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percentages
Point estimate	-1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.4
upper limit	0.9

Primary: Percentage of Participants With CK >=10 x ULN With Muscle Spasms	
End point title	Percentage of Participants With CK >=10 x ULN With Muscle Spasms
End point description:	
Participants had CK assessed throughout the 52 week treatment period. Participants who had any CK level that was >=10 x ULN and had associated muscle spasms were recorded. The UNLs for males and females were 207 U/L and 169 U/L, respectively.	
End point type	Primary
End point timeframe:	
Up to 52 weeks	

End point values	Anacetrapib 100 mg - Safety Population	Placebo - Safety Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	202	101		
Units: Percentage of Participants				
number (not applicable)	0	1		

Statistical analyses

Statistical analysis title	Difference in Percentages Between Groups
Comparison groups	Anacetrapib 100 mg - Safety Population v Placebo - Safety Population
Number of subjects included in analysis	303
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.157
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percentages
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.4
upper limit	0.9

Primary: Percentage of Participants Adjudicated Cardiovascular (CV) SAE

End point title	Percentage of Participants Adjudicated Cardiovascular (CV) SAE

End point description:

An AE or suspected adverse reaction is was considered an SAE if it results in any of the following outcomes: death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect. All events were adjudicated by an expert committee independent of the Sponsor. Participants that experienced adjudicated SAEs of CV death, Non-fatal stroke, non-fatal myocardial infarction, or unstable angina were recorded.

End point type	Primary

End point timeframe:

Up to 52 weeks

End point values	Anacetrapib 100 mg - Safety Population	Placebo - Safety Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	203	102		
Units: Percentage of Participants				
number (not applicable)	1.5	0		

Statistical analyses

Statistical analysis title	Difference in Percentages Between Groups
Comparison groups	Anacetrapib 100 mg - Safety Population v Placebo - Safety Population
Number of subjects included in analysis	305
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.218
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percentages
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	4.3

Primary: Percentage of Participants Who Died From Any Cause - Treatment Period

End point title	Percentage of Participants Who Died From Any Cause - Treatment Period

End point description:

Participants who died from any cause were recorded. All deaths were adjudicated by an expert committee independent of the Sponsor.

End point type	Primary

End point timeframe:

Up to 52 weeks

End point values	Anacetrapib 100 mg - Safety Population	Placebo - Safety Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	203	102		
Units: Percentage of Participants				
number (not applicable)	0	0		

Statistical analyses

Statistical analysis title	Difference in Percentages Between Groups
Comparison groups	Anacetrapib 100 mg - Safety Population v Placebo - Safety Population
Number of subjects included in analysis	305
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percentages
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.6
upper limit	1.9

Secondary: Percent Change From Baseline in High-density Lipoprotein-cholesterol (HDL-C)

End point title	Percent Change From Baseline in High-density Lipoprotein-cholesterol (HDL-C)

End point description:

HDL-C levels measured at baseline and after 52 weeks of treatment.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Anacetrapib 100 mg- Efficacy Population	Placebo - Efficacy Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	173	88		
Units: Percentage Change				
least squares mean (confidence interval 95%)	105.8 (101.1 to 110.6)	3.7 (-2.8 to 10.3)		

Statistical analyses

Statistical analysis title	Difference in Least Squares Mean Changes
Statistical analysis description:	
Between group comparison of percent change from baseline performed using Constrained Longitudinal Data Analysis (cLDA) model with terms for treatment, time, and the interaction of time by treatment. Analysis population defined as participants who receive at least 1 dose of study treatment and have baseline and at least 1 post-randomization observation for the analysis endpoint.	
Comparison groups	Anacetrapib 100 mg- Efficacy Population v Placebo - Efficacy Population
Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Difference in Least Squares Means
Point estimate	102.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	94.2
upper limit	110.1

Secondary: Percent Change From Baseline in non- HDL-C

End point title	Percent Change From Baseline in non- HDL-C
End point description:	
Non-HDL-C levels measured at baseline and after 52 weeks of treatment.	
End point type	Secondary
End point timeframe:	
Baseline and Week 52	

End point values	Anacetrapib 100 mg- Efficacy Population	Placebo - Efficacy Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	173	88		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-32 (-35.1 to -28.9)	4.4 (0.1 to 8.8)		

Statistical analyses

Statistical analysis title	Difference in Least Squares Mean Change
Statistical analysis description:	
Between group comparison of percent change from baseline performed using Constrained Longitudinal Data Analysis (cLDA) model with terms for treatment, time, and the interaction of time by treatment. Analysis population defined as participants who receive at least 1 dose of study treatment and have baseline and at least 1 post-randomization observation for the analysis endpoint.	
Comparison groups	Anacetrapib 100 mg- Efficacy Population v Placebo - Efficacy Population
Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Difference in Least Squares Means
Point estimate	-36.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-41.7
upper limit	-31.1

Secondary: Percent Change From Baseline in Apolipoprotein B (Apo B)

End point title	Percent Change From Baseline in Apolipoprotein B (Apo B)
End point description:	
Apo B levels measured at baseline and after 52 weeks of treatment	
End point type	Secondary
End point timeframe:	
Baseline and Week 52	

End point values	Anacetrapib 100 mg- Efficacy Population	Placebo - Efficacy Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	173	88		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-19.6 (-22.5 to -16.8)	5.2 (1.3 to 9.1)		

Statistical analyses

Statistical analysis title	Difference in Least Squares Mean Change
Statistical analysis description:	
Between group comparison of percent change from baseline performed using Constrained Longitudinal Data Analysis (cLDA) model with terms for treatment, time, and the interaction of time by treatment. Analysis population defined as participants who receive at least 1 dose of study treatment and have baseline and at least 1 post-randomization observation for the analysis endpoint.	
Comparison groups	Anacetrapib 100 mg- Efficacy Population v Placebo - Efficacy Population
Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Difference in Least Squares Means
Point estimate	-24.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.5
upper limit	-20.1

Secondary: Percent Change From Baseline in Apolipoprotein A1 (Apo-A1)

End point title	Percent Change From Baseline in Apolipoprotein A1 (Apo-A1)
End point description:	
Apo A-1 levels measured at baseline and after 52 weeks of treatment.	
End point type	Secondary
End point timeframe:	
Baseline and Week 52	

End point values	Anacetrapib 100 mg- Efficacy Population	Placebo - Efficacy Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	173	88		
Units: Percentage Change				
least squares mean (confidence interval 95%)	35.8 (33 to 38.6)	2.9 (-1 to 6.8)		

Statistical analyses

Statistical analysis title	Difference in Least Squares Mean Change
Statistical analysis description:	
Between group comparison of percent change from baseline performed using Constrained Longitudinal Data Analysis (cLDA) model with terms for treatment, time, and the interaction of time by treatment. Analysis population defined as participants who receive at least 1 dose of study treatment and have baseline and at least 1 post-randomization observation for the analysis endpoint.	
Comparison groups	Anacetrapib 100 mg- Efficacy Population v Placebo - Efficacy Population
Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Difference in Least Squares Means
Point estimate	32.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	28.2
upper limit	37.6

Secondary: Percent Change From Baseline in Lipoprotein(a) (Lp[a])

End point title	Percent Change From Baseline in Lipoprotein(a) (Lp[a])
End point description:	
Lp(a) levels measured at baseline and after 52 weeks of treatment.	
End point type	Secondary
End point timeframe:	
Baseline and Week 52	

End point values	Anacetrapib 100 mg- Efficacy Population	Placebo - Efficacy Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	174	88		
Units: Percentage Change				
median (confidence interval 95%)	-31.8 (-37.4 to -26.3)	0 (-5.1 to 5.1)		

Statistical analyses

Statistical analysis title	Difference in Median Change

Statistical analysis description:

Between group comparison of percent change from baseline performed using Hodges-Lehmann estimate of the median difference between treatments with a corresponding distribution-free CI based on Wilcoxon's rank sum test. Analysis population defined as participants who receive at least 1 dose of study treatment and have baseline and at least 1 post-randomization observation for the analysis endpoint.

Comparison groups	Anacetrapib 100 mg- Efficacy Population v Placebo - Efficacy Population
Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Wilcoxon's rank sum test
Parameter estimate	Median difference (final values)
Point estimate	-27.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-34.7
upper limit	-21.2

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 64 weeks	
Adverse event reporting additional description:	
Safety Population included all participants who received at least 1 dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	MK-0859 100 mg (52-week Treatment Phase)
Reporting group description:	
one tablet of anacetrapib 100 mg once daily with a meal for 52 weeks	
Reporting group title	Placebo (52-week Treatment Phase)
Reporting group description:	
one tablet of placebo for anacetrapib 100 mg once daily with a meal for 52 weeks	
Reporting group title	MK-0859 100 mg (12-week Reversal Phase)
Reporting group description:	
Completers and non-completers who were administered anacetrapib in treatment period and entered reversal period.	
Reporting group title	Placebo (12-week Reversal Phase)
Reporting group description:	
Completers and non-completers who were administered placebo in treatment period and entered reversal period.	

Serious adverse events	MK-0859 100 mg (52-week Treatment Phase)	Placebo (52-week Treatment Phase)	MK-0859 100 mg (12-week Reversal Phase)
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 203 (8.87%)	10 / 102 (9.80%)	3 / 196 (1.53%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 203 (0.49%)	0 / 102 (0.00%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	1 / 203 (0.49%)	1 / 102 (0.98%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Colon cancer			
subjects affected / exposed	0 / 203 (0.00%)	1 / 102 (0.98%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 203 (0.00%)	1 / 102 (0.98%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Device malfunction			
subjects affected / exposed	1 / 203 (0.49%)	0 / 102 (0.00%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug resistance			
subjects affected / exposed	1 / 203 (0.49%)	0 / 102 (0.00%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Medical device discomfort			
subjects affected / exposed	1 / 203 (0.49%)	0 / 102 (0.00%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Uterovaginal prolapse			
subjects affected / exposed	1 / 203 (0.49%)	0 / 102 (0.00%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 203 (0.49%)	0 / 102 (0.00%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			

subjects affected / exposed	1 / 203 (0.49%)	0 / 102 (0.00%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Emotional distress			
subjects affected / exposed	0 / 203 (0.00%)	1 / 102 (0.98%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Gastrointestinal anastomotic leak			
subjects affected / exposed	0 / 203 (0.00%)	1 / 102 (0.98%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	1 / 203 (0.49%)	0 / 102 (0.00%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	0 / 203 (0.00%)	0 / 102 (0.00%)	1 / 196 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 203 (0.00%)	0 / 102 (0.00%)	1 / 196 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 203 (0.00%)	0 / 102 (0.00%)	1 / 196 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	4 / 203 (1.97%)	0 / 102 (0.00%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Angina unstable			
subjects affected / exposed	1 / 203 (0.49%)	0 / 102 (0.00%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 203 (0.00%)	1 / 102 (0.98%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 203 (0.00%)	0 / 102 (0.00%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 203 (0.00%)	1 / 102 (0.98%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	1 / 203 (0.49%)	1 / 102 (0.98%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cardiomyopathy			
subjects affected / exposed	1 / 203 (0.49%)	0 / 102 (0.00%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	1 / 203 (0.49%)	0 / 102 (0.00%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular fibrillation			
subjects affected / exposed	0 / 203 (0.00%)	1 / 102 (0.98%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			

Loss of consciousness			
subjects affected / exposed	0 / 203 (0.00%)	1 / 102 (0.98%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine with aura			
subjects affected / exposed	0 / 203 (0.00%)	0 / 102 (0.00%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 203 (0.00%)	0 / 102 (0.00%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Pancreatitis			
subjects affected / exposed	1 / 203 (0.49%)	0 / 102 (0.00%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 203 (0.49%)	0 / 102 (0.00%)	1 / 196 (0.51%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	1 / 203 (0.49%)	0 / 102 (0.00%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Endocarditis			
subjects affected / exposed	1 / 203 (0.49%)	0 / 102 (0.00%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral discitis			

subjects affected / exposed	1 / 203 (0.49%)	0 / 102 (0.00%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 203 (0.00%)	1 / 102 (0.98%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 203 (0.49%)	0 / 102 (0.00%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 203 (0.00%)	1 / 102 (0.98%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo (12-week Reversal Phase)		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 95 (2.11%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Breast cancer			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colon cancer			

subjects affected / exposed	0 / 95 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Prostate cancer				
subjects affected / exposed	0 / 95 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Device malfunction				
subjects affected / exposed	0 / 95 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Drug resistance				
subjects affected / exposed	0 / 95 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Medical device discomfort				
subjects affected / exposed	0 / 95 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Uterovaginal prolapse				
subjects affected / exposed	0 / 95 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Asthma				
subjects affected / exposed	0 / 95 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleurisy				

subjects affected / exposed	0 / 95 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Emotional distress			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Gastrointestinal anastomotic leak			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Post procedural haemorrhage			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thoracic vertebral fracture			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute myocardial infarction			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Angina pectoris			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Angina unstable			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Coronary artery disease			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ischaemic cardiomyopathy			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial ischaemia			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ventricular fibrillation			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			

Loss of consciousness				
subjects affected / exposed	0 / 95 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Migraine with aura				
subjects affected / exposed	1 / 95 (1.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
subjects affected / exposed	1 / 95 (1.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Pancreatitis				
subjects affected / exposed	0 / 95 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholelithiasis				
subjects affected / exposed	0 / 95 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Renal colic				
subjects affected / exposed	0 / 95 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Endocarditis				
subjects affected / exposed	0 / 95 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intervertebral discitis				

subjects affected / exposed	0 / 95 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	MK-0859 100 mg (52-week Treatment Phase)	Placebo (52-week Treatment Phase)	MK-0859 100 mg (12-week Reversal Phase)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	87 / 203 (42.86%)	41 / 102 (40.20%)	0 / 196 (0.00%)
Nervous system disorders			
Headache			
subjects affected / exposed	16 / 203 (7.88%)	6 / 102 (5.88%)	0 / 196 (0.00%)
occurrences (all)	19	7	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	16 / 203 (7.88%)	9 / 102 (8.82%)	0 / 196 (0.00%)
occurrences (all)	19	10	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	12 / 203 (5.91%)	2 / 102 (1.96%)	0 / 196 (0.00%)
occurrences (all)	15	2	0
Myalgia			

subjects affected / exposed	18 / 203 (8.87%)	4 / 102 (3.92%)	0 / 196 (0.00%)
occurrences (all)	26	5	0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	2 / 203 (0.99%)	6 / 102 (5.88%)	0 / 196 (0.00%)
occurrences (all)	2	7	0
Influenza			
subjects affected / exposed	20 / 203 (9.85%)	11 / 102 (10.78%)	0 / 196 (0.00%)
occurrences (all)	22	11	0
Nasopharyngitis			
subjects affected / exposed	40 / 203 (19.70%)	19 / 102 (18.63%)	0 / 196 (0.00%)
occurrences (all)	50	21	0

Non-serious adverse events	Placebo (12-week Reversal Phase)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 95 (0.00%)		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences (all)	0		
Influenza			

subjects affected / exposed	0 / 95 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 May 2012	AM1: changed the LDL-C method for the primary efficacy endpoint from direct method to beta quantification method and for women of child- bearing potential to report pregnancy anytime during the 2 year time period after stopping study medication.
01 November 2013	AM2: updated the contraception guidance to women of child- bearing potential and to implement pregnancy follow-up on an annual basis for up to 4 years after the last dose of study medication.
19 February 2015	AM3: Updated the annual pregnancy follow-up period for women of child-bearing potential (WOCBP) from 4 years to 5 years after the last dose of anacetrapib. Also contraception guidance for WOCBP was extended from 4 to 5 years after last dose of anacetrapib.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported