



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

Summary

EudraCT number	2011-004525-27
Trial protocol	GB DE NL ES CZ
Global end of trial date	13 November 2018

Results information

Result version number	v2 (current)
This version publication date	17 November 2019
First version publication date	19 July 2015
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	0859-020
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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, 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	13 November 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 February 2014
Global end of trial reached?	Yes
Global end of trial date	13 November 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study is to evaluate the efficacy and tolerability of adding anacetrapib to ongoing statin therapy in participants with heterozygous familial hypercholesterolemia (HeFH).

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: -

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	0

wk	
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:

This study was conducted at 26 study centers. Participants were to complete a 2-week placebo run-in period, a 52-week randomized treatment phase and a 12-week reversal phase (safety follow-up).

Pre-assignment

Screening details:

The study enrolled participants who were 18 to 80 years old, had 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.

Period 1

Period 1 title	Overall Period (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	Anacetrapib 100 mg

Arm description:

Participants were administered one tablet of 100 mg anacetrapib orally once daily with a meal for 52 weeks during the treatment phase.

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
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Arm description:

Participants were administered one matching placebo tablet orally once daily with a meal for 52 weeks during the treatment phase.

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	-
Did not take study medication	1	-
Adverse event, non-fatal	12	5
Withdrawal by Subject	11	7
Lost to follow-up	-	1
Protocol deviation	5	1

Baseline characteristics

Reporting groups

Reporting group title	Anacetrapib 100 mg
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Reporting group description:

Participants were administered one tablet of 100 mg anacetrapib orally once daily with a meal for 52 weeks during the treatment phase.

Reporting group title	Placebo
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Reporting group description:

Participants were administered one matching placebo tablet orally once daily with a meal for 52 weeks during the treatment phase.

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

Age Continuous Units: years arithmetic mean standard deviation	55.0 ± 11.8	55.7 ± 11.9	-
Gender Categorical Units: Subjects			
Female	84	52	136
Male	120	50	170
Race/Ethnicity Units: Subjects			
Asian	2	0	2
Black or African American	0	1	1
Multi-racial	3	1	4
White	199	100	299

End points

End points reporting groups

Reporting group title	Anacetrapib 100 mg
Reporting group description: Participants were administered one tablet of 100 mg anacetrapib orally once daily with a meal for 52 weeks during the treatment phase.	
Reporting group title	Placebo
Reporting group description: Participants were administered one matching placebo tablet orally once daily with a meal for 52 weeks during the treatment phase.	

Primary: Percent Change from Baseline in Low-Density Lipoprotein Cholesterol (LDL-C) - Treatment Phase

End point title	Percent Change from Baseline in Low-Density Lipoprotein Cholesterol (LDL-C) - Treatment Phase
End point description: LDL-C levels were measured at baseline and week 52 (or at discontinuation) using a beta quantification method. The Treatment Phase was the period from the date of the participant's first dose of study treatment (randomization visit, Visit 3) to the participant's last visit on treatment (discontinuation visit or Visit 8 [Week 52]). The full analysis set (FAS) population consisted of all randomized participants who received at least one dose of study treatment, had at least one post randomization observation for the analysis endpoint subsequent to at least one dose of study treatment and had baseline data for those analyses that require baseline data.	
End point type	Primary
End point timeframe: Baseline and Week 52	

End point values	Anacetrapib 100 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	85		
Units: Percent Change				
least squares mean (confidence interval 95%)	-36.0 (-39.5 to -32.5)	3.7 (-1.2 to 8.6)		

Statistical analyses

Statistical analysis title	Superiority
Comparison groups	Anacetrapib 100 mg v Placebo
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 (LS) Means
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 - Treatment Phase

End point title	Percentage of Participants with Any Adverse Event - Treatment Phase
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End point description:

An adverse event (AE) or experience was any unfavorable and unintended change in the structure (signs), function (symptoms), or chemistry (laboratory data) of the body temporally associated with any use of a study treatment, whether or not considered related to the use of the study treatment. Any worsening of a preexisting condition which was temporally associated with the use of the study treatment is also an AE. The percentage of participants with any adverse event during the treatment phase is presented.

End point type	Primary
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End point timeframe:

Up to 52 weeks

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

Statistical analyses

Statistical analysis title	Adverse Events: Anacetrapib 100 mg vs. Placebo
Comparison groups	Anacetrapib 100 mg v Placebo
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 Treatment-Related Adverse Event - Treatment Phase

End point title	Percentage of Participants with Any Treatment-Related Adverse Event - Treatment Phase
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End point description:

An AE was defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study treatment, whether or not considered related to the use of the treatment. Any worsening of a preexisting condition which was temporally associated with the use of the study treatment was also an AE. AEs reported by the investigator as definitely, probably or possibly related to study treatment were considered treatment-related. The percentage of participants with any treatment-related adverse event during the treatment phase is presented. The APaT population consisted of all randomized participants who received at least one dose of study treatment.

End point type	Primary
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End point timeframe:

Up to 52 weeks

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

Statistical analyses

Statistical analysis title	Treatment AE: Anacetrapib 100 mg vs. Placebo
Comparison groups	Anacetrapib 100 mg v Placebo
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 - Treatment Phase

End point title	Percentage of Participants with Any Serious Adverse Event - Treatment Phase
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End point description:

A serious adverse experience (SAE) was any adverse event that occurred at any dose that resulted in death or was life threatening, resulted in a persistent or significant disability/incapacity, resulted in or

prolonged an existing inpatient hospitalization, or was a congenital anomaly/birth defect. The percentage of participants with any serious adverse event during the treatment phase is presented. The APaT population consisted of all randomized participants who received at least one dose of study treatment.

End point type	Primary
End point timeframe:	
Up to 52 weeks	

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

Statistical analyses

Statistical analysis title	SAEs: Anacetrapib 100 mg vs. Placebo
Comparison groups	Anacetrapib 100 mg v Placebo
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 Discontinuing Study Treatment Due to an Adverse Event - Treatment Phase

End point title	Percentage of Participants Discontinuing Study Treatment Due to an Adverse Event - Treatment Phase
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End point description:

An adverse event (AE) was defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study treatment, whether or not considered related to the use of the drug. Any worsening of a preexisting condition which was temporally associated with the use of the study drug was also an AE. The percentage of participants who discontinued study treatment due to an AE during the treatment phase is presented. The APaT population consists of all randomized participants who received at least one dose of study treatment.

End point type	Primary
End point timeframe:	
Up to 52 weeks	

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

Statistical analyses

Statistical analysis title	Anacetrapib 100 mg vs. Placebo
Comparison groups	Anacetrapib 100 mg v Placebo
Number of subjects included in analysis	305
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.168
Method	Miettinen & 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 Changes in Systolic Blood Pressure (SBP) ≥ 10 mm Hg

End point title	Percentage of Participants with Changes in Systolic Blood Pressure (SBP) ≥ 10 mm Hg
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End point description:

Participants had SBP assessed at baseline and throughout the 52-week treatment period. Percentage of participants who had a SBP reading that was ≥ 10 mm Hg higher than their baseline SBP for any assessment performed during the treatment phase is presented. The analysis population consisted of all randomized participants who received at least one dose of study treatment and had at least one post-baseline test result that met pre-determined criteria.

End point type	Primary
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End point timeframe:

Up to 52 weeks

End point values	Anacetrapib 100 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	101		
Units: Percentage of Participants				
number (not applicable)	45.0	53.5		

Statistical analyses

Statistical analysis title	SBP \geq 10: Anacetrapib 100 mg vs. Placebo
Comparison groups	Anacetrapib 100 mg v Placebo
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 Changes in SBP \geq 15 mm Hg

End point title	Percentage of Participants with Changes in SBP \geq 15 mm Hg
End point description:	Participants had SBP assessed at baseline and throughout the 52-week treatment period. The percentage of participants who had a SBP reading that was \geq 15 mm Hg higher than their baseline SBP for any assessment performed during the treatment phase is presented. The analysis population consisted of all randomized participants who received at least one dose of study treatment and had at least one post-baseline test result that met pre-determined criteria.
End point type	Primary
End point timeframe:	
Up to 52 weeks	

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

Statistical analyses

Statistical analysis title	SBP \geq 15: Anacetrapib 100 mg vs. Placebo
Comparison groups	Anacetrapib 100 mg v Placebo
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 Changes in Diastolic Blood Pressure (DBP) \geq 10 mm Hg

End point title	Percentage of Participants with Changes in Diastolic Blood Pressure (DBP) \geq 10 mm Hg
End point description:	
Participants had DBP assessed at baseline and throughout the 52-week treatment period. The percentage of participants who had a DBP reading that was \geq 10 mm Hg higher than their baseline DBP for any assessment performed during the treatment phase is presented. The analysis population consisted of all randomized participants who received at least one dose of study treatment and had at least one post-baseline test result that met pre-determined criteria.	
End point type	Primary
End point timeframe:	
Up to 52 weeks	

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

Statistical analyses

Statistical analysis title	DBP \geq 10: Anacetrapib 100 mg vs. Placebo
Comparison groups	Anacetrapib 100 mg v Placebo

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)
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End point description:

Participants had sodium levels assessed throughout the 52-week treatment period. The percentage of participants who had any sodium level that was greater than the ULN of 145 mEq/L during the treatment phase is presented. The analysis population consisted of all randomized participants who received at least one dose of study treatment and had at least one post-baseline test result that met pre-determined criteria.

End point type	Primary
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End point timeframe:

Up to 52 weeks

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

Statistical analyses

Statistical analysis title	Sodium > ULN: Anacetrapib 100 mg vs. Placebo
Comparison groups	Anacetrapib 100 mg v Placebo
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. The percentage of participants who had any chloride level that was > the ULN of 110 mEq/L during the treatment phase is presented. The analysis population consisted of all randomized participants who received at least one dose of study treatment and had at least one post-baseline test result that met pre-determined criteria.	
End point type	Primary
End point timeframe:	
Up to 52 weeks	

End point values	Anacetrapib 100 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	101		
Units: Percentage of Participants				
number (not applicable)	0.5	0.0		

Statistical analyses

Statistical analysis title	Chloride > ULN: Anacetrapib 100 mg vs. Placebo
Comparison groups	Anacetrapib 100 mg v Placebo
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)
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End point description:

Participants had potassium levels assessed throughout the 52-week treatment period. The percentage of participants who had any potassium level that was < the LLN of 3.5 mEq/L during the treatment phase is presented. The analysis population consisted of all randomized participants who received at least one dose of study treatment and had at least one post-baseline test result that met pre-determined criteria.

End point type	Primary
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End point timeframe:

Up to 52 weeks

End point values	Anacetrapib 100 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	101		
Units: Percentage of Participants				
number (not applicable)	1.5	1.0		

Statistical analyses

Statistical analysis title	Potassium < LLN: Anacetrapib 100 mg vs.Placebo
Comparison groups	Anacetrapib 100 mg v Placebo
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
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End point description:

Participants had bicarbonate levels assessed throughout the 52-week treatment period. The percentage of participants who had any bicarbonate level that was > the ULN of 33 mEq/L during the treatment phase is presented. The analysis population consisted of all randomized participants who received at least one dose of study treatment and had at least one post-baseline test result that met pre-determined criteria.

End point type	Primary
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End point timeframe:

Up to 52 weeks

End point values	Anacetrapib 100 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	101		
Units: Percentage of Participants				
number (not applicable)	0.0	0.0		

Statistical analyses

Statistical analysis title	Bicarbonate > ULN: Anacetrapib 100 mg vs. Placebo
Comparison groups	Anacetrapib 100 mg v Placebo
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 Changes in Alanine Aminotransferase (ALT) and/or Aspartate Aminotransferase (AST) of $\geq 3 \times$ ULN

End point title	Percentage of Participants with Consecutive Changes in Alanine Aminotransferase (ALT) and/or Aspartate Aminotransferase (AST) of $\geq 3 \times$ ULN
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End point description:

Participants had AST and ALT levels assessed throughout the 52-week treatment period. The percentage of participants who had 2 consecutive assessments of either AST or ALT that were $3 \times$ ULN or greater during the treatment phase is presented. The analysis population consisted of all randomized participants who received at least one dose of study treatment and had at least one post-baseline test result that met pre-determined criteria.

End point type	Primary
End point timeframe:	
Up to 52 weeks	

End point values	Anacetrapib 100 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	101		
Units: Percentage of Participants				
number (not applicable)	1.5	1.0		

Statistical analyses

Statistical analysis title	ALT/AST $\geq 3 \times$ ULN: Anacetrapib 100 mg vs. Placebo
Comparison groups	Anacetrapib 100 mg v Placebo
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) Level $\geq 10 \times$ ULN

End point title	Percentage of Participants with Creatine Kinase (CK) Level $\geq 10 \times$ ULN
End point description:	Participants had CK levels assessed throughout the 52-week treatment period. The percentage of participants who had any CK level that was $\geq 10 \times$ ULN during the treatment phase is presented. The analysis population consisted of all randomized participants who received at least one dose of study treatment and had at least one post-baseline test result that met pre-determined criteria.
End point type	Primary
End point timeframe:	
Up to 52 weeks	

End point values	Anacetrapib 100 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	101		
Units: Percentage of Participants				
number (not applicable)	0.0	1.0		

Statistical analyses

Statistical analysis title	CK $\geq 10 \times$ ULN: Anacetrapib 100 mg vs. Placebo
Comparison groups	Anacetrapib 100 mg v Placebo
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 Level $\geq 10 \times$ ULN with Muscle Spasms

End point title	Percentage of Participants with CK Level $\geq 10 \times$ ULN with Muscle Spasms
End point description:	
Participants had CK levels assessed throughout the 52-week treatment period. The percentage of participants who had any CK level that was $\geq 10 \times$ ULN and had associated muscle spasms during the treatment phase is presented. The analysis population consisted of all randomized participants who received at least one dose of study treatment and had at least one post-baseline test result that met pre-determined criteria.	
End point type	Primary
End point timeframe:	
Up to 52 weeks	

End point values	Anacetrapib 100 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	101		
Units: Percentage of Participants				
number (not applicable)	0.0	1.0		

Statistical analyses

Statistical analysis title	CK $\geq 10 \times$ ULN & Sp: Anacetrapib 100 mg vs. Placebo
Comparison groups	Anacetrapib 100 mg v Placebo

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 was considered an SAE if it resulted 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. The percentage of participants that experienced adjudicated SAEs of CV death, non-fatal stroke, non-fatal myocardial infarction, or unstable angina during the treatment phase is presented. The APaT population consisted of all randomized participants who received at least one dose of study treatment.	
End point type	Primary
End point timeframe:	
Up to 52 weeks	

End point values	Anacetrapib 100 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	102		
Units: Percentage of Participants				
number (not applicable)	1.5	0.0		

Statistical analyses

Statistical analysis title	CV SAE: Anacetrapib 100 mg vs. Placebo
Comparison groups	Anacetrapib 100 mg v Placebo
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	0.218

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 Phase

End point title	Percentage of Participants Who Died from Any Cause - Treatment Phase
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End point description:

The percentage of participants who died from any cause during the treatment phase is presented. All deaths were adjudicated by an expert committee independent of the Sponsor. The APaT population consisted of all randomized participants who received at least one dose of study treatment.

End point type	Primary
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End point timeframe:

Up to 52 weeks

End point values	Anacetrapib 100 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	102		
Units: Percentage of Participants				
number (not applicable)	0.0	0.0		

Statistical analyses

Statistical analysis title	Any Cause Death: Anacetrapib 100 mg vs. Placebo
Comparison groups	Anacetrapib 100 mg v Placebo
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 Levels

End point title	Percent Change from Baseline in High-Density Lipoprotein Cholesterol Levels
End point description: The efficacy of adding anacetrapib 100 mg relative to placebo on plasma concentrations of high-density lipoprotein cholesterol (HDL-C) was evaluated at Week 0 (start of treatment phase) and Week 52 (end of treatment phase) or at discontinuation. The FAS population consisted of all randomized participants who received at least one dose of study treatment and had at least one post randomization observation for the analysis endpoint subsequent to at least one dose of study treatment, and had baseline data for those analyses that require baseline data.	
End point type	Secondary
End point timeframe: Baseline and Week 52	

End point values	Anacetrapib 100 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	88		
Units: Percent Change				
least squares mean (full range (min-max))	105.8 (101.1 to 110.6)	3.7 (-2.8 to 10.3)		

Statistical analyses

Statistical analysis title	HDL: Anacetrapib 100 mg vs. Placebo
Comparison groups	Anacetrapib 100 mg v Placebo
Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Difference in Least Squares (LS) 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-High-Density Lipoprotein Cholesterol Levels

End point title	Percent Change from Baseline in Non-High-Density Lipoprotein Cholesterol Levels
End point description: The efficacy of adding anacetrapib 100 mg was evaluated relative to placebo on plasma concentrations of non-high-density lipoprotein cholesterol (HDL-C) for the FAS population at Week 0 (start of treatment phase) and Week 52 (end of treatment phase) or at discontinuation. The FAS population consisted of all randomized participants who received at least one dose of study treatment and had at least one post randomization observation for the analysis endpoint subsequent to at least one dose of study treatment,	

and had baseline data for those analyses that require baseline data.

End point type	Secondary
End point timeframe:	
Baseline and Week 52	

End point values	Anacetrapib 100 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	88		
Units: Percent Change				
least squares mean (full range (min-max))	-32.0 (-35.1 to -28.9)	4.4 (0.1 to 8.8)		

Statistical analyses

Statistical analysis title	Non-HDL: Anacetrapib 100 mg vs. Placebo
Comparison groups	Anacetrapib 100 mg v Placebo
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 LS 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 (Apo) B Levels

End point title	Percent Change from Baseline in Apolipoprotein (Apo) B Levels
End point description:	
The efficacy of adding anacetrapib 100 mg was evaluated relative to placebo on plasma concentrations of apolipoprotein (Apo) B for the FAS population at Week 0 (start of treatment phase) and Week 52 (end of treatment phase) or at discontinuation. The FAS population consisted of all randomized participants who received at least one dose of study treatment and had at least one post randomization observation for the analysis endpoint subsequent to at least one dose of study treatment, and had baseline data for those analyses that require baseline data.	
End point type	Secondary
End point timeframe:	
Baseline and Week 52	

End point values	Anacetrapib 100 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	88		
Units: Percent Change				
number (confidence interval 95%)	-19.6 (-22.5 to -16.8)	5.2 (1.3 to 9.1)		

Statistical analyses

Statistical analysis title	Apo B: Anacetrapib 100 mg vs. Placebo
Comparison groups	Anacetrapib 100 mg v Placebo
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 LS 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 (Apo) A-1 Levels

End point title	Percent Change from Baseline in Apolipoprotein (Apo) A-1 Levels
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End point description:

The efficacy of adding anacetrapib 100 mg was evaluated relative to placebo on plasma concentrations of Apo A-1 for the FAS population at Week 0 (start of treatment phase) and Week 52 (end of treatment phase) or at discontinuation. The FAS population consisted of all randomized participants who received at least one dose of study treatment and had at least one post randomization observation for the analysis endpoint subsequent to at least one dose of study treatment, and had baseline data for those analyses that require baseline data.

End point type	Secondary
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End point timeframe:

Baseline and Week 52

End point values	Anacetrapib 100 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	88		
Units: Percent Change				
number (confidence interval 95%)	35.8 (33.0 to 38.6)	2.9 (-1.0 to 6.8)		

Statistical analyses

Statistical analysis title	Apo A-1: Anacetrapib 100 mg vs. Placebo
Comparison groups	Anacetrapib 100 mg v Placebo
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 LS 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]) Levels

End point title	Percent Change from Baseline in Lipoprotein(a) (Lp[a]) Levels
End point description:	
The efficacy of adding anacetrapib 100 mg was evaluated relative to placebo on plasma concentrations of lipoprotein(a) (Lp[a]) for the FAS population at Week 0 (start of treatment phase) and Week 52 (end of treatment phase) or at discontinuation. The FAS population consisted of all randomized participants who received at least one dose of study treatment and had at least one post randomization observation for the analysis endpoint subsequent to at least one dose of study treatment, and had baseline data for those analyses that require baseline data.	
End point type	Secondary
End point timeframe:	
Baseline and Week 52	

End point values	Anacetrapib 100 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	174	88		
Units: Percent Change				
number (confidence interval 95%)	-31.8 (-37.4 to -26.3)	0.0 (-5.1 to 5.1)		

Statistical analyses

Statistical analysis title	Lp[a]: Anacetrapib 100 mg vs. Placebo
Statistical analysis description:	
Hodges-Lehmann estimate of the median difference between treatments with a corresponding distribution-free confidence interval (CI) based on Wilcoxon's rank sum test.	
Comparison groups	Anacetrapib 100 mg v Placebo
Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean 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: All participants who received at least 1 dose of study treatment. The treatment phase included AEs in 52-week period (first dose to last visit of treatment). The reversal phase included AEs in 12-week period after treatment phase (~Week 64).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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Reporting groups

Reporting group title	Anacetrapib 100 mg - Treatment Phase
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Reporting group description:

Participants were administered one tablet of 100 mg anacetrapib orally once daily with a meal for 52 weeks.

Reporting group title	Placebo - Treatment Phase
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Reporting group description:

Participants were administered one matching placebo tablet orally once daily with a meal for 52 weeks.

Reporting group title	Anacetrapib 100 mg - Reversal Phase
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Reporting group description:

Safety data that was reported during the 12-week period from the day after the treatment phase to the participant's last visit (discontinuation visit or week 64).

Reporting group title	Placebo - Reversal Phase
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Reporting group description:

Safety data that was reported during the 12-week period from the day after the treatment phase to the participant's last visit (discontinuation visit or week 64).

Serious adverse events	Anacetrapib 100 mg - Treatment Phase	Placebo - Treatment Phase	Anacetrapib 100 mg - 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			
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
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
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
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
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%)	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
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 - 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			
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			
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			
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			
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		
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	Anacetrapib 100 mg - Treatment Phase	Placebo - Treatment Phase	Anacetrapib 100 mg - 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 - 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 March 2012	AM 1: 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	AM 2: 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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

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Notes: