Clinical trial results:
A Worldwide, Multicenter, Double-Blind, Randomized, Placebo-Controlled, 12-Week Study to Assess the Efficacy and Tolerability of Anacetrapib When Added to Ongoing Lipid-Lowering Therapy in Adult Patients with Homozygous Familial Hypercholesterolemia (HoFH)

Summary

EudraCT number	2012-002434-37
Trial protocol	GB NO CZ IT
Global end of trial date	05 June 2014

Results information

Result version number	v1 (current)
This version publication date	13 April 2016
First version publication date	29 July 2015

Trial information

Trial identification

Sponsor protocol code	MK-0859-042

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01841684
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 June 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 June 2014
Global end of trial reached?	Yes
Global end of trial date	05 June 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This study will evaluate the safety and effect of anacetrapib on low-density lipoprotein-cholesterol (LDL-C) when added to ongoing lipid-lowering therapy. The primary hypothesis is that treatment with anacetrapib 100 mg for 12 weeks will lower LDL-C to a greater extent than treatment with placebo.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 June 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	3 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Norway: 2
Worldwide total number of subjects	2
EEA total number of subjects	2

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)	2
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study was terminated due to lack of enrollment after 2 participants were randomized. No planned efficay or safety analyses were performed due to low sample number.

Pre-assignment

Screening details:

Male or female (not of child bearing potential) and 18 years of age or older diagnosed with HoFH by genotyping. Other inclusion and exclusion criteria applied.

Period 1

Period 1 title	Treatment 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

Arm description:

Participants receive anacetrapib 100 mg orally once daily for 12 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 orally once daily for 12 weeks.

Arm title	Placebo

Arm description:

Participants received placebo for anacetrapib once daily for 12 weeks

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

Dosage and administration details:

one placebo tablet orally once daily for 12 weeks.

Number of subjects in period 1	Anacetrapib	Placebo
Started	1	1
Completed	0	0
Not completed	1	1
Study terminated	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Anacetrapib
Reporting group description:	
Participants receive anacetrapib 100 mg orally once daily for 12 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo for anacetrapib once daily for 12 weeks	

Reporting group values	Anacetrapib	Placebo	Total
Number of subjects	1	1	2
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	43	33	
full range (min-max)	43 to 43	33 to 33	-
Gender categorical Units: Subjects			
Female	0	0	0
Male	1	1	2

End points

End points reporting groups

Reporting group title	Anacetrapib
Reporting group description:	
Participants receive anacetrapib 100 mg orally once daily for 12 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo for anacetrapib once daily for 12 weeks	

Primary: Percent change from Baseline in Low-density Lipoprotein-Cholesterol (LDL-C) using beta-quantification method

End point title	Percent change from Baseline in Low-density Lipoprotein-Cholesterol (LDL-C) using beta-quantification method[1]
End point description:	
LDL-C levels measured at baseline and after 12 weeks of treatment using beta quantification method	
End point type	Primary
End point timeframe:	
Baseline and Week 12	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Study terminated early. No planned statistical analyses were performed.

End point values	Anacetrapib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: Percentage Change				
least squares mean (confidence interval 95%)	(to)	(to)		

Notes:

[2] - Study terminated early. No planned analyses were performed.

[3] - Study terminated early. No planned analyses were performed.

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Alanine Transaminase (ALT) or Aspartate Aminotransferase (AST) Consecutive Elevations ≥3x Upper Limit of Normal (ULN)

End point title	Number of Participants with Alanine Transaminase (ALT) or Aspartate Aminotransferase (AST) Consecutive Elevations ≥3x Upper Limit of Normal (ULN)[4]
End point description:	
Participants had AST and ALT levels assessed throughout the 12 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:	
12 weeks	

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Study terminated early. No planned statistical analyses were performed.

End point values	Anacetrapib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[5]	0[6]		
Units: Participants				

Notes:

[5] - Study terminated early. No planned analyses were performed.

[6] - Study terminated early. No planned analyses were performed.

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Creatine Phosphokinase Elevations ≥10xULN with or without Muscle Symptoms

End point title	Number of Participants with Creatine Phosphokinase Elevations ≥10xULN with or without Muscle Symptoms[7]

End point description:

Participants had creatine phosphokinase (CPK) assessed throughout the 12 week treatment period. Participants who had any CPK 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:

12 weeks

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Study terminated early. No planned statistical analyses were performed.

End point values	Anacetrapib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[8]	0[9]		
Units: Participants				

Notes:

[8] - Study terminated early. No planned analyses were performed.

[9] - Study terminated early. No planned analyses were performed.

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Sodium, Chloride, or Bicarbonate Elevations >ULN or Potassium Levels < Lower Limit of Normal (LLN)

End point title	Number of Participants with Sodium, Chloride, or Bicarbonate Elevations >ULN or Potassium Levels < Lower Limit of Normal (LLN)[10]

End point description:

Participants had sodium, chloride, bicarbonate, and potassium levels assessed throughout the 12 week treatment period. Participants who had any sodium chloride, or bicarbonate levels that was > the ULN or had a potassium level < LLN were summarized. The ULNs for sodium, chloride, and bicarbonate were 145 mEq/L, 110 mEq/L, and 33 mEq/L, respectively. The LLN for potassium was 3.5 mEq/L.

End point type	Primary

End point timeframe:

12 weeks

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Study terminated early. No planned statistical analyses were performed.

End point values	Anacetrapib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[11]	0[12]		
Units: Participants				

Notes:

[11] - Study terminated early. No planned analyses were performed.

[12] - Study terminated early. No planned analyses were performed.

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Pre-specified Adjudicated Cardiovascular Serious Adverse Events or Death from Any Cause

End point title	Number of Participants with Pre-specified Adjudicated Cardiovascular Serious Adverse Events or Death from Any Cause[13]

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 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 acongenital 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 or died from any cause were recorded.

End point type	Primary

End point timeframe:

12 weeks

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Study terminated early. No planned statistical analyses were performed.

End point values	Anacetrapib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[14]	0[15]		
Units: Participants				

Notes:

[14] - Study terminated early. No planned analyses were performed.

[15] - Study terminated early. No planned analyses were performed.

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Significant Increase in Blood Pressure

End point title	Number of Participants with Significant Increase in Blood

	Pressure[16]

End point description:

Sitting blood pressure was assessed throughout the 12 week treatment period. Participants with an increase in sitting systolic blood pressure (SiSBP) of ≥10 mmHg and/or ≥15 mmHg and/or an increase in sitting diastolic blood pressure (SiSBP) of ≥10 mmHg were recorded.

End point type	Primary

End point timeframe:

12 weeks

Notes:

[16] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Study terminated early. No planned statistical analyses were performed.

End point values	Anacetrapib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[17]	0[18]		
Units: Participants				

Notes:

[17] - Study terminated early. No planned analyses were performed.

[18] - Study terminated early. No planned analyses were performed.

Statistical analyses

No statistical analyses for this end point

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 12 weeks of treatment.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Anacetrapib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[19]	0[20]		
Units: Percentage change				
least squares mean (confidence interval 95%)	(to)	(to)		

Notes:

[19] - Study terminated early. No planned analyses were performed.

[20] - Study terminated early. No planned analyses were performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in Apolipoprotein A-I (apoA-I)

End point title	Percent Change from Baseline in Apolipoprotein A-I (apoA-I)

End point description:

Apo A-1 levels measured at baseline and after 12 weeks of treatment.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Anacetrapib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[21]	0[22]		
Units: Percentage Change				
least squares mean (confidence interval 95%)	(to)	(to)		

Notes:

[21] - Study terminated early. No planned analyses were performed.

[22] - Study terminated early. No planned analyses were performed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: up to 12 weeks	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups	
Reporting group title	Placebo
Reporting group description: All participants who received at least one dose of placebo.	
Reporting group title	Anacetrapib 100 mg
Reporting group description: All participants who received at least one dose of Anacetrapib 100 mg	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: None of the participants experienced a non-serious adverse event.

Serious adverse events	Placebo	Anacetrapib 100 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	1 / 1 (100.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Cardiac disorders			
Angina unstable			
subjects affected / exposed	0 / 1 (0.00%)	1 / 1 (100.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Influenza			
subjects affected / exposed	0 / 1 (0.00%)	1 / 1 (100.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Anacetrapib 100 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 May 2013	Amendment 1: provided new data on the pharmacokinetic (PK) properties of anacetrapib and related changes to eligibility criteria. The 52-week open label extension phase was removed from the study and a 12-week follow-up period was added. The addition of serial PK measurements during the follow-up period was to be performed to determine the accumulation and clearance of the compound in the HoFH population.
20 November 2013	Amendment 3: removed the 30% cap limiting the number of participants being treated with LDL apheresis that were allowed to enroll in the trial. All participants who were receiving LDL apheresis treatment for at least 8 weeks prior to randomization were allowed to enter the study.

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.

Study was terminated early due to poor enrollment after 2 participants were randomly assigned to a treatment arm and dosed. No planned analyses were performed.

Notes: