



Clinical trial results:

A Randomized, Double-Blind, Parallel-Group, Placebo-Controlled Efficacy and Safety Study of Ezetimibe Monotherapy in Children (Ages 6 to 10 Years) With Primary Hypercholesterolemia (Heterozygous Familial and Nonfamilial)

Summary

EudraCT number	2008-006271-70
Trial protocol	NL FR IT GR Outside EU/EEA
Global end of trial date	13 April 2012

Results information

Result version number	v1 (current)
This version publication date	15 March 2016
First version publication date	19 April 2015

Trial information

Trial identification

Sponsor protocol code	P05522
-----------------------	--------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00867165
WHO universal trial number (UTN)	-
Other trial identifiers	Merck Study Number: MK-0653-170

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)	Yes
EMA paediatric investigation plan number(s)	EMA-000007-PIP01-07
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 April 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 April 2012
Global end of trial reached?	Yes
Global end of trial date	13 April 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Determine the effect of ezetimibe 10mg/day compared to placebo on the reduction of low-density lipoprotein cholesterol (LDL-C) from baseline to 12 weeks of treatment in children ≥ 6 to ≤ 10 years old with primary hypercholesterolemia (heterozygous familial hypercholesterolemia [HeFH] and nonfamilial).

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	21 May 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects**Subjects enrolled per country**

Country: Number of subjects enrolled	Netherlands: 15
Country: Number of subjects enrolled	Norway: 8
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Greece: 12
Country: Number of subjects enrolled	Italy: 14
Country: Number of subjects enrolled	Colombia: 15
Country: Number of subjects enrolled	Israel: 4
Country: Number of subjects enrolled	Canada: 34
Country: Number of subjects enrolled	United States: 31
Worldwide total number of subjects	138
EEA total number of subjects	54

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)	138
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were to complete a 5-week placebo run-in and a 12-week treatment period

Pre-assignment

Screening details:

The study enrolled participants 6 to 10 years of age, with a genotype-confirmed or clinical diagnosis of heterozygous familial hypercholesterolemia (HeFH). 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, Carer

Arms

Are arms mutually exclusive?	Yes
------------------------------	-----

Arm title	Ezetimibe
------------------	-----------

Arm description:

Ezetimibe 10-mg tablet once daily for 12 weeks

Arm type	Experimental
Investigational medicinal product name	Ezetimibe
Investigational medicinal product code	
Other name	MK-0653, SCH 058235
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

one 10-mg tablet administered once daily during the 12-week double-blind treatment period

Arm title	Placebo
------------------	---------

Arm description:

Placebo to match ezetimibe 10-mg tablet once daily for 12 weeks

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

Dosage and administration details:

Administered once daily during the 5-week, single-blind, placebo run-in and diet stabilization period and 12-week double-blind treatment period.

Number of subjects in period 1	Ezetimibe	Placebo
Started	93	45
Completed	89	45
Not completed	4	0
Consent withdrawn by subject	1	-
Adverse event, non-fatal	3	-

Baseline characteristics

Reporting groups

Reporting group title	Ezetimibe
-----------------------	-----------

Reporting group description:

Ezetimibe 10-mg tablet once daily for 12 weeks

Reporting group title	Placebo
-----------------------	---------

Reporting group description:

Placebo to match ezetimibe 10-mg tablet once daily for 12 weeks

Reporting group values	Ezetimibe	Placebo	Total
Number of subjects	93	45	138
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	8.2 ± 1.7	8.5 ± 1.6	-
Gender categorical Units: Subjects			
Female	52	27	79
Male	41	18	59
Hypercholesterolemia Stratum Units: Subjects			
HeFH	84	41	125
Non-familial	9	4	13

End points

End points reporting groups

Reporting group title	Ezetimibe
Reporting group description: Ezetimibe 10-mg tablet once daily for 12 weeks	
Reporting group title	Placebo
Reporting group description: Placebo to match ezetimibe 10-mg tablet once daily for 12 weeks	
Subject analysis set title	Ezetimibe 10 mg - Efficacy
Subject analysis set type	Full analysis
Subject analysis set description: All randomized participants who took at least one dose of study medication and had a baseline value and at least one valid post-baseline evaluation.	
Subject analysis set title	Placebo - Efficacy
Subject analysis set type	Full analysis
Subject analysis set description: All randomized participants who took at least one dose of study medication and had a baseline value and at least one valid post-baseline evaluation.	

Primary: Percentage Change from Baseline in Low-density Lipoprotein Cholesterol (LDL-C) at Week 12

End point title	Percentage Change from Baseline in Low-density Lipoprotein Cholesterol (LDL-C) at Week 12
End point description: Serum LDL-C levels calculated at baseline and after 12 weeks of study drug administration. LDL-C were calculated by the method of Friedewald equation, $LDL-C = Total\ Cholesterol\ (TC) - (High-density\ lipoprotein\ cholesterol\ [HDL-C] + triglyceride\ [TG]/5)$.	
End point type	Primary
End point timeframe: Baseline and Week 12	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	85	42		
Units: Percentage change				
least squares mean (confidence interval 95%)	-27.7 (-30.8 to -24.59)	-0.95 (-4.94 to 3.04)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description: Analysis performed using an analysis of covariance (ANCOVA) mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy

Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	< 0.001 ^[2]
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-26.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.8
upper limit	-22.69

Notes:

[1] - Primary hypothesis is that after 12 weeks of treatment, ezetimibe 10 mg/day monotherapy will reduce LDL-C to a greater extent than placebo in children 6 to 10 years old with primary hypercholesterolemia (HeFH and nonfamilial).

[2] - p-value of ≤ 0.05 for the treatment group comparison was considered supportive of the primary study hypothesis.

Secondary: Percentage Change from Baseline in Total Cholesterol (TC) at Week 12

End point title	Percentage Change from Baseline in Total Cholesterol (TC) at Week 12
End point description: Serum TC levels measured using enzymatic methods at baseline and after 12 weeks of study drug administration.	
End point type	Secondary
End point timeframe: Baseline and Week 12	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	85	42		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-20.74 (-23.29 to -18.18)	0.19 (-3.07 to 3.44)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description: Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Placebo - Efficacy v Ezetimibe 10 mg - Efficacy

Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-20.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.2
upper limit	-17.65

Secondary: Percentage Change from Baseline in Apolipoprotein B (Apo B) at Week 12

End point title	Percentage Change from Baseline in Apolipoprotein B (Apo B) at Week 12
End point description:	Serum Apo B measured at baseline and after 12 weeks of study drug administration. Apo B levels were measured at baseline and ONLY at one post-baseline time point; Week 12.
End point type	Secondary
End point timeframe:	Baseline and Week 12

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	85	42		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-21.66 (-24.94 to -18.38)	-1.42 (-5.55 to 2.7)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description:	Analysis performed using an ANCOVA mixed model with fixed effects for baseline Apo B, treatment, gender, and primary diagnosis.
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-20.24

Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.02
upper limit	-16.45

Secondary: Percentage Change from Baseline in High-density Lipoprotein Cholesterol (HDL-C) at Week 12

End point title	Percentage Change from Baseline in High-density Lipoprotein Cholesterol (HDL-C) at Week 12
End point description: Serum HDL-C levels measured by photometry after precipitation at baseline and after 12 weeks of study drug administration.	
End point type	Secondary
End point timeframe: Baseline and Week 12	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	85	42		
Units: Percentage change				
least squares mean (confidence interval 95%)	2.11 (-2.27 to 6.48)	1.41 (-4.14 to 6.96)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description: Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.807
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.97
upper limit	6.36

Secondary: Percentage Change from Baseline in Non-HDL-C at Week 12

End point title	Percentage Change from Baseline in Non-HDL-C at Week 12
-----------------	---

End point description:

Serum Non-HDL-C calculated at baseline and after 12 weeks of study drug administration. Non-HDL-C values were calculated as follows: Non-HDL-C (mg/dL) = TC - HDL-C.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline and Week 12

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	85	42		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-25.47 (-28.45 to -22.49)	0.28 (-3.52 to 4.08)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
----------------------------	---

Statistical analysis description:

Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.

Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-25.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.59
upper limit	-21.91

Secondary: Percentage Change from Baseline in Triglycerides (TG) at Week 12

End point title	Percentage Change from Baseline in Triglycerides (TG) at Week 12
-----------------	--

End point description:

Serum TG levels measured using enzymatic methods at baseline and after 12 weeks of study drug administration.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline and Week 12

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	85	42		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-6.23 (-12.73 to 0.75)	8.44 (-2.03 to 20.03)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
----------------------------	---

Statistical analysis description:

Analysis was based on log-transformed data using a constrained longitudinal data analysis (cLDA) model with terms for treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and the interaction of treatment by study week. The difference in Least-Square (LS) Means was based on the difference in the back transformed model-based LS means and the associated confidence interval is calculated using the Delta method.

Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.021
Method	constrained longitudinal data analysis
Parameter estimate	Difference in Least Squares Means
Point estimate	-14.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.35
upper limit	-2

Secondary: Percentage Change From Baseline in LDL-C at Week 2

End point title	Percentage Change From Baseline in LDL-C at Week 2
-----------------	--

End point description:

Serum LDL-C levels calculated at baseline and after 2 weeks of study drug administration. LDL-C were calculated by the method of Friedewald equation, $LDL-C = Total\ Cholesterol\ (TC) - (High-density\ lipoprotein\ cholesterol\ [HDL-C] + triglyceride\ [TG]/5)$.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline and Week 2

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	43		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-24.75 (-27.8 to -21.69)	0.23 (-3.74 to 4.2)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description: Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Mean
Point estimate	-24.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.95
upper limit	-20.99

Secondary: Percentage Change From Baseline in LDL-C at Week 4

End point title	Percentage Change From Baseline in LDL-C at Week 4
End point description: Serum LDL-C levels calculated at baseline and after 4 weeks of study drug administration. LDL-C were calculated by the method of Friedewald equation, LDL-C = Total Cholesterol (TC) - (High-density lipoprotein cholesterol [HDL-C] + triglyceride [TG]/5).	
End point type	Secondary
End point timeframe: Baseline and Week 4	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	43		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-26.93 (-29.81 to -24.05)	-2.99 (-6.66 to 0.68)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description:	
Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-23.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.49
upper limit	-20.39

Secondary: Percentage Change From Baseline in LDL-C at Week 8

End point title	Percentage Change From Baseline in LDL-C at Week 8
End point description:	
Serum LDL-C levels calculated at baseline and after 8 weeks of study drug administration. LDL-C were calculated by the method of Friedewald equation, LDL-C = Total Cholesterol (TC) – (High-density lipoprotein cholesterol [HDL-C] + triglyceride [TG]/5).	
End point type	Secondary
End point timeframe:	
Baseline and Week 8	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	44		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-27.22 (-30.3 to -24.15)	0.49 (-3.46 to 4.43)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description: Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-27.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.7
upper limit	-23.73

Secondary: Percentage Change from Baseline in TC at Week 2

End point title	Percentage Change from Baseline in TC at Week 2
End point description: Serum TC levels measured using enzymatic methods at baseline and after 2 weeks of study drug administration.	
End point type	Secondary
End point timeframe: Baseline and Week 2	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	43		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-18.69 (-21.21 to -16.18)	1.4 (-1.83 to 4.63)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description: Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-20.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.3
upper limit	-16.89

Secondary: Percentage Change From Baseline in TC at Week 4

End point title	Percentage Change From Baseline in TC at Week 4
End point description: Serum TC levels measured using enzymatic methods at baseline and after 4 weeks of study drug administration.	
End point type	Secondary
End point timeframe: Baseline and Week 4	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	43		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-20.57 (-23.05 to -18.08)	-0.29 (-3.45 to 2.86)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description: Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy

Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-20.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.39
upper limit	-17.15

Secondary: Percentage Change From Baseline in TC at Week 8

End point title	Percentage Change From Baseline in TC at Week 8
End point description:	
Serum TC levels measured using enzymatic methods at baseline and after 8 weeks of study drug administration.	
End point type	Secondary
End point timeframe:	
Baseline and Week 8	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	44		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-20.84 (-23.4 to -18.27)	0.54 (-2.73 to 3.81)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description:	
Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-21.37

Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.67
upper limit	-18.08

Secondary: Percentage Change From Baseline in HDL-C at Week 2

End point title	Percentage Change From Baseline in HDL-C at Week 2
End point description: Serum HDL-C levels measured by photometry after precipitation at baseline and after 2 weeks of study drug administration.	
End point type	Secondary
End point timeframe: Baseline and Week 2	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	43		
Units: Percentage Change				
least squares mean (confidence interval 95%)	0.01 (-4.28 to 4.3)	0.96 (-4.51 to 6.43)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description: Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.733
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.46
upper limit	4.55

Secondary: Percentage Change From Baseline in HDL-C at Week 4

End point title	Percentage Change From Baseline in HDL-C at Week 4
-----------------	--

End point description:

Serum HDL-C levels measured by photometry after precipitation at baseline and after 4 weeks of study drug administration.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline and Week 4

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	43		
Units: Percentage Change				
least squares mean (confidence interval 95%)	0.86 (-3.69 to 5.42)	0.33 (-5.54 to 6.19)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
----------------------------	---

Statistical analysis description:

Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.

Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.863
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.59
upper limit	6.66

Secondary: Percentage Change From Baseline in HDL-C at Week 8

End point title	Percentage Change From Baseline in HDL-C at Week 8
-----------------	--

End point description:

Serum HDL-C levels measured by photometry after precipitation at baseline and after 8 weeks of study

drug administration.

End point type	Secondary
End point timeframe:	
Baseline and Week 8	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	44		
Units: Percentage Change				
least squares mean (confidence interval 95%)	1.41 (-2.95 to 5.77)	-0.52 (-6.04 to 5)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description:	
Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Placebo - Efficacy v Ezetimibe 10 mg - Efficacy
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.501
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	1.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.71
upper limit	7.56

Secondary: Percentage Change From Baseline in Non-HDL-C at Week 2

End point title	Percentage Change From Baseline in Non-HDL-C at Week 2
End point description:	
Serum Non-HDL-C calculated at baseline and after 2 weeks of study drug administration. Non-HDL-C values were calculated as follows: Non-HDL-C (mg/dL) = TC - HDL-C.	
End point type	Secondary
End point timeframe:	
Baseline and Week 2	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	43		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-22.54 (-25.41 to -19.67)	1.64 (-2.03 to 5.3)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description:	
Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-24.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.78
upper limit	-20.58

Secondary: Percentage Change From Baseline in Non-HDL-C at Week 4

End point title	Percentage Change From Baseline in Non-HDL-C at Week 4
End point description:	
Serum Non-HDL-C calculated at baseline and after 4 weeks of study drug administration. Non-HDL-C values were calculated as follows: Non-HDL-C (mg/dL) = TC – HDL-C.	
End point type	Secondary
End point timeframe:	
Baseline and Week 4	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	43		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-24.94 (-27.75 to -22.14)	-0.33 (-3.88 to 3.22)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description: Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-24.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.06
upper limit	-21.16

Secondary: Percentage Change From Baseline in Non-HDL-C at Week 8

End point title	Percentage Change From Baseline in Non-HDL-C at Week 8
End point description: Serum Non-HDL-C calculated at baseline and after 8 weeks of study drug administration. Non-HDL-C values were calculated as follows: Non-HDL-C (mg/dL) = TC - HDL-C.	
End point type	Secondary
End point timeframe: Baseline and Week 8	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	44		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-25.41 (-28.37 to -22.45)	1.14 (-2.63 to 4.92)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description: Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Placebo - Efficacy v Ezetimibe 10 mg - Efficacy
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-26.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.35
upper limit	-22.75

Secondary: Percentage Change From Baseline in TG at Week 2

End point title	Percentage Change From Baseline in TG at Week 2
End point description: Serum TG levels measured using enzymatic methods at baseline and after 2 weeks of study drug administration.	
End point type	Secondary
End point timeframe: Baseline and Week 2	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	43		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-3.9 (-10.66 to 3.37)	5.83 (-4.76 to 17.59)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description: Analysis was based on log-transformed data using a cLDA model with terms for treatment, gender, primary diagnosis, study week, and the interaction of treatment by study week. The difference in LS Means was based on the difference in the back transformed model-based LS means and the associated confidence interval is calculated using the Delta method.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy

Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.137
Method	Constrained longitudinal data analysis
Parameter estimate	Difference in Least-Squares Means
Point estimate	-9.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.73
upper limit	3.27

Secondary: Percentage Change From Baseline in TG at Week 4

End point title	Percentage Change From Baseline in TG at Week 4
End point description:	
Serum TG levels measured using enzymatic methods at baseline and after 4 weeks of study drug administration.	
End point type	Secondary
End point timeframe:	
Baseline and Week 4	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	43		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-5.54 (-11.05 to 0.31)	9.65 (0.6 to 19.53)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description:	
Analysis was based on log-transformed data using a cLDA model with terms for treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and the interaction of treatment by study week. The difference in LS Means was based on the difference in the back transformed model-based LS means and the associated confidence interval is calculated using the Delta method.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.005
Method	Constrained longitudinal data analysis
Parameter estimate	Difference in Least-Squares Means
Point estimate	-15.19

Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.05
upper limit	-4.34

Secondary: Percentage Change From Baseline in TG at Week 8

End point title	Percentage Change From Baseline in TG at Week 8
End point description: Serum TG levels measured using enzymatic methods at baseline and after 8 weeks of study drug administration.	
End point type	Secondary
End point timeframe: Baseline and Week 8	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	44		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-9.99 (-16.28 to -3.21)	-1.38 (-11.02 to 9.31)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description: Analysis was based on log-transformed data using a cLDA model with terms for treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and the interaction of treatment by study week. The difference in LS Means was based on the difference in the back transformed model-based LS means and the associated confidence interval is calculated using the Delta method.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.149
Method	Constrained longitudinal data analysis
Parameter estimate	Difference in Least-Squares Means
Point estimate	-8.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.44
upper limit	3.23

Secondary: Percentage Change from Baseline in Apolipoprotein A-I (Apo A-I) at Week 12

End point title	Percentage Change from Baseline in Apolipoprotein A-I (Apo A-I) at Week 12
-----------------	--

End point description:

Serum Apo A-I levels measured at baseline and after 12 weeks of study drug administration. Apo A-I levels were measured at baseline and ONLY at one post-baseline time point; Week 12.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline and Week 12

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	85	42		
Units: Percentage Change				
least squares mean (confidence interval 95%)	1.8 (-1.86 to 5.46)	3.71 (-0.87 to 8.3)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
----------------------------	---

Statistical analysis description:

Analysis performed using an ANCOVA mixed model with fixed effects for baseline Apo A-I, treatment, gender, and primary diagnosis.

Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
-------------------	---

Number of subjects included in analysis	127
---	-----

Analysis specification	Pre-specified
------------------------	---------------

Analysis type	other
---------------	-------

P-value	= 0.373
---------	---------

Method	ANCOVA
--------	--------

Parameter estimate	Difference in Least-Squares Means
--------------------	-----------------------------------

Point estimate	-1.91
----------------	-------

Confidence interval

level	95 %
-------	------

sides	2-sided
-------	---------

lower limit	-6.15
-------------	-------

upper limit	2.32
-------------	------

Secondary: Percentage Change from Baseline in TC:HDL-C Ratio at Week 2

End point title	Percentage Change from Baseline in TC:HDL-C Ratio at Week 2
-----------------	---

End point description:	
Serum TC:HDL-C Ratio calculated at baseline and after 2 weeks of study drug administration.	
End point type	Secondary
End point timeframe:	
Baseline and Week 2	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	43		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-17.21 (-21.08 to -13.34)	2.56 (-2.37 to 7.48)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
-----------------------------------	---

Statistical analysis description:

Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.

Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-19.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.7
upper limit	-14.82

Secondary: Percentage Change From Baseline in TC:HDL-C Ratio at Week 4

End point title	Percentage Change From Baseline in TC:HDL-C Ratio at Week 4
End point description:	
Serum TC:HDL-C Ratio calculated at baseline and after 4 weeks of study drug administration.	
End point type	Secondary
End point timeframe:	
Baseline and Week 4	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	43		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-19.36 (-23.16 to -15.56)	1.48 (-3.3 to 6.25)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description:	
Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-20.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.59
upper limit	-16.07

Secondary: Percentage Change From Baseline in TC:HDL-C Ratio at Week 8

End point title	Percentage Change From Baseline in TC:HDL-C Ratio at Week 8
End point description:	
Serum TC:HDL-C Ratio calculated at baseline and after 8 weeks of study drug administration.	
End point type	Secondary
End point timeframe:	
Baseline and Week 8	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	44		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-20.07 (-24.2 to -15.94)	3.41 (-1.87 to 8.7)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description:	
Analysis performed using an ANCOVA mixed model with fixed effects for treatment, baseline covariate corresponding to the analysis parameter, gender, primary diagnosis, study week and treatment by study week interaction.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-23.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29
upper limit	-17.97

Secondary: Percentage Change From Baseline in TC:HDL-C Ratio at Week 12

End point title	Percentage Change From Baseline in TC:HDL-C Ratio at Week 12
End point description:	
Serum TC:HDL-C Ratio calculated at baseline and after 12 weeks of study drug administration.	
End point type	Secondary
End point timeframe:	
Baseline and Week 12	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	85	42		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-21.09 (-24.98 to -17.19)	1.2 (-3.7 to 6.11)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description: Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-22.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.25
upper limit	-17.34

Secondary: Percentage Change From Baseline in LDL-C:HDL-C Ratio at Week 2

End point title	Percentage Change From Baseline in LDL-C:HDL-C Ratio at Week 2
End point description: Serum LDL-C:HDL-C Ratio calculated at baseline and after 2 weeks of study drug administration.	
End point type	Secondary
End point timeframe: Baseline and Week 2	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	43		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-23.35 (-27.69 to -19.01)	1.15 (-4.35 to 6.65)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description: Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-24.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.88
upper limit	-19.12

Secondary: Percentage Change From Baseline in LDL-C:HDL-C Ratio at Week 4

End point title	Percentage Change From Baseline in LDL-C:HDL-C Ratio at Week 4
End point description: Serum LDL-C:HDL-C Ratio calculated at baseline and after 4 weeks of study drug administration.	
End point type	Secondary
End point timeframe: Baseline and Week 4	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	42		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-25.72 (-30.12 to -21.33)	-0.57 (-6.14 to 5)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description: Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy

Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-25.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.69
upper limit	-19.62

Secondary: Percentage Change From Baseline in LDL-C:HDL-C Ratio at Week 8

End point title	Percentage Change From Baseline in LDL-C:HDL-C Ratio at Week 8
End point description:	Serum LDL-C:HDL-C Ratio calculated at baseline and after 8 weeks of study drug administration.
End point type	Secondary
End point timeframe:	Baseline and Week 8

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	43		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-26.43 (-31.21 to -21.66)	2.87 (-3.28 to 9.02)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description:	Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-29.31

Confidence interval	
level	95 %
sides	2-sided
lower limit	-35.71
upper limit	-22.91

Secondary: Percentage Change From Baseline in LDL-C:HDL-C Ratio at Week 12

End point title	Percentage Change From Baseline in LDL-C:HDL-C Ratio at Week 12
End point description: Serum LDL-C:HDL-C Ratio calculated at baseline and after 12 weeks of study drug administration.	
End point type	Secondary
End point timeframe: Baseline and Week 12	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	85	42		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-28.01 (-32.65 to -23.36)	0.34 (-5.57 to 6.25)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description: Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Mean
Point estimate	-28.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-34.41
upper limit	-22.29

Secondary: Percentage Change From Baseline in Apo B:Apo A-I Ratio at Week 12

End point title	Percentage Change From Baseline in Apo B:Apo A-I Ratio at Week 12
-----------------	---

End point description:

Serum Apo B:Apo A-I Ratio calculated at baseline and after 12 weeks of study drug administration

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline and Week 12

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	85	42		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-22.16 (-26.13 to -18.19)	-2.87 (-7.84 to 2.09)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
----------------------------	---

Statistical analysis description:

Analysis performed using an ANCOVA mixed model with fixed effects for baseline Apo B:Apo A-I ratio, treatment, gender, and primary diagnosis.

Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
-------------------	---

Number of subjects included in analysis	127
---	-----

Analysis specification	Pre-specified
------------------------	---------------

Analysis type	other
---------------	-------

P-value	< 0.001
---------	---------

Method	ANCOVA
--------	--------

Parameter estimate	Difference in Least-Squares Means
--------------------	-----------------------------------

Point estimate	-19.28
----------------	--------

Confidence interval

level	95 %
-------	------

sides	2-sided
-------	---------

lower limit	-23.87
-------------	--------

upper limit	-14.7
-------------	-------

Secondary: Percentage Change from Baseline in High-sensitivity C-reactive protein (hs-CRP) at Week 4

End point title	Percentage Change from Baseline in High-sensitivity C-reactive protein (hs-CRP) at Week 4
-----------------	---

End point description:	
Plasma hs-CRP measured at baseline and after 4 weeks of study drug administration.	
End point type	Secondary
End point timeframe:	
Baseline and Week 4	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	43		
Units: Percentage Change				
least squares mean (confidence interval 95%)	10 (-15.65 to 43.45)	56.11 (7.68 to 126.32)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
-----------------------------------	---

Statistical analysis description:

Analysis was based on log-transformed data using a cLDA model with terms for treatment, gender, primary diagnosis (HeFH, Non-familial), study week (4 and 12), and the interaction of treatment by study week. The difference in LS Means was based on the difference in the back transformed model-based LS means and the associated confidence interval is calculated using the Delta method.

Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.116
Method	Constrained longitudinal data analysis
Parameter estimate	Difference in Least-Squares Means
Point estimate	-46.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-108.14
upper limit	15.92

Secondary: Percentage Change from Baseline in High-sensitivity C-reactive protein (hs-CRP) at Week 12

End point title	Percentage Change from Baseline in High-sensitivity C-reactive protein (hs-CRP) at Week 12
-----------------	--

End point description:

Plasma hs-CRP measured at baseline and after 12 weeks of study drug administration.

End point type	Secondary
End point timeframe:	
Baseline and Week 12	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	85	42		
Units: Percentage Change				
least squares mean (confidence interval 95%)	9.35 (-13.47 to 38.19)	-7.92 (-33.48 to 27.46)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description:	
Analysis was based on log-transformed data using a cLDA model with terms for treatment, gender, primary diagnosis (HeFH, Non-familial), study week (4 and 12), and the interaction of treatment by study week. The difference in LS Means was based on the difference in the back transformed model-based LS means and the associated confidence interval is calculated using the Delta method.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.382
Method	Constrained longitudinal data analysis
Parameter estimate	Difference in Least-Squares Means
Point estimate	17.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.46
upper limit	55

Secondary: Percent Change From Baseline in Sitosterol at Week 2

End point title	Percent Change From Baseline in Sitosterol at Week 2
End point description:	
Plasma sitosterol measured at baseline and after 2 weeks of study drug administration.	
End point type	Secondary
End point timeframe:	
Baseline and Week 2	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	89	43		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-50.2 (-54.65 to -45.76)	-0.59 (-6.26 to 5.08)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description:	
Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-49.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-55.36
upper limit	-43.87

Secondary: Percentage Change From Baseline in Sitosterol at Week 4

End point title	Percentage Change From Baseline in Sitosterol at Week 4
End point description:	
Plasma sitosterol measured at baseline and after 4 weeks of study drug administration.	
End point type	Secondary
End point timeframe:	
Baseline and Week 4	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	87	43		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-58.82 (-63.04 to -54.61)	-0.3 (-5.52 to 4.93)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description: Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-58.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-63.67
upper limit	-53.38

Secondary: Percentage Change From Baseline in Sitosterol at Week 8

End point title	Percentage Change From Baseline in Sitosterol at Week 8
End point description: Plasma sitosterol measured at baseline and after 8 weeks of study drug administration.	
End point type	Secondary
End point timeframe: Baseline and Week 8	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	86	44		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-61.59 (-66.39 to -56.78)	-0.57 (-6.69 to 5.56)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description: Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-61.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-67.51
upper limit	-54.53

Secondary: Percentage Change From Baseline in Sitosterol at Week 12

End point title	Percentage Change From Baseline in Sitosterol at Week 12
End point description: Plasma sitosterol measured at baseline and after 12 weeks of study drug administration.	
End point type	Secondary
End point timeframe: Baseline and Week 12	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	82	41		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-60.65 (-67.39 to -53.92)	2.09 (-7.01 to 11.18)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description: Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy

Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-62.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-73.22
upper limit	-52.26

Secondary: Percentage Change From Baseline in Campesterol at Week 2

End point title	Percentage Change From Baseline in Campesterol at Week 2
End point description:	Plasma campesterol measured at baseline and after 2 weeks of study drug administration.
End point type	Secondary
End point timeframe:	Baseline and Week 2

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	89	43		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-53.87 (-57.99 to -49.74)	-4.38 (-9.66 to 0.9)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description:	Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-49.48

Confidence interval	
level	95 %
sides	2-sided
lower limit	-54.83
upper limit	-44.14

Secondary: Percentage Change From Baseline in Campesterol at Week 4

End point title	Percentage Change From Baseline in Campesterol at Week 4
End point description: Plasma campesterol measured at baseline and after 4 weeks of study drug administration.	
End point type	Secondary
End point timeframe: Baseline and Week 4	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	87	43		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-62.27 (-66.21 to -58.32)	-4.28 (-9.2 to 0.65)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description: Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-57.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	-62.87
upper limit	-53.11

Secondary: Percentage Change From Baseline in Campesterol at Week 8

End point title	Percentage Change From Baseline in Campesterol at Week 8
-----------------	--

End point description:

Plasma campesterol measured at baseline and after 8 weeks of study drug administration.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline and Week 8

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	86	44		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-66.79 (-71.21 to -62.37)	-4.19 (-9.83 to 1.45)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
----------------------------	---

Statistical analysis description:

Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.

Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-62.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-68.54
upper limit	-56.66

Secondary: Percentage Change From Baseline in Campesterol at Week 12

End point title	Percentage Change From Baseline in Campesterol at Week 12
-----------------	---

End point description:

Plasma campesterol measured at baseline and after 12 weeks of study drug administration.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline and Week 12

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	82	41		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-67.59 (-73.68 to -61.5)	-2.92 (-11.15 to 5.31)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description:	
Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-64.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-74.11
upper limit	-55.23

Secondary: Percentage Change From Baseline in Cholesterol at Week 2

End point title	Percentage Change From Baseline in Cholesterol at Week 2
End point description:	
Plasma cholesterol measured at baseline and after 2 weeks of study drug administration.	
End point type	Secondary
End point timeframe:	
Baseline and Week 2	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	89	43		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-25.44 (-30.3 to -20.59)	-7.09 (-13.29 to -0.9)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description:	
Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Placebo - Efficacy v Ezetimibe 10 mg - Efficacy
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-18.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.7
upper limit	-11.99

Secondary: Percentage Change From Baseline in Cholestanol at Week 4

End point title	Percentage Change From Baseline in Cholestanol at Week 4
End point description:	
Plasma cholestanol measured at baseline and after 4 weeks of study drug administration.	
End point type	Secondary
End point timeframe:	
Baseline and Week 4	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	87	43		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-27.4 (-31.95 to -22.85)	-1.79 (-7.42 to 3.85)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description: Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-25.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.2
upper limit	-20.02

Secondary: Percentage Change From Baseline in Cholesterol at Week 8

End point title	Percentage Change From Baseline in Cholesterol at Week 8
End point description: Plasma cholesterol measured at baseline and after 8 weeks of study drug administration.	
End point type	Secondary
End point timeframe: Baseline and Week 8	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	86	44		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-29.19 (-33.98 to -24.39)	-0.44 (-6.44 to 5.56)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description: Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-28.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-34.89
upper limit	-22.59

Secondary: Percentage Change From Baseline in Cholesterol at Week 12

End point title	Percentage Change From Baseline in Cholesterol at Week 12
End point description: Plasma cholesterol measured at baseline and after 12 weeks of study drug administration.	
End point type	Secondary
End point timeframe: Baseline and Week 12	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	82	41		
Units: Percentage Change				
least squares mean (confidence interval 95%)	-28.71 (-34.44 to -22.99)	3.42 (-4.07 to 10.92)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description: Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy

Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	-32.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-40.38
upper limit	-23.9

Secondary: Percentage Change From Baseline in Lathosterol at Week 2

End point title	Percentage Change From Baseline in Lathosterol at Week 2
End point description:	Plasma lathosterol measured at baseline and after 2 weeks of study drug administration.
End point type	Secondary
End point timeframe:	Baseline and Week 2

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	89	43		
Units: Percentage Change				
least squares mean (confidence interval 95%)	34.07 (24.68 to 43.45)	14.06 (2.22 to 25.9)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description:	Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Mean
Point estimate	20.01

Confidence interval	
level	95 %
sides	2-sided
lower limit	8.1
upper limit	31.91

Secondary: Percentage Change From Baseline in Lathosterol at Week 4

End point title	Percentage Change From Baseline in Lathosterol at Week 4
End point description: Plasma lathosterol measured at baseline and after 4 weeks of study drug administration.	
End point type	Secondary
End point timeframe: Baseline and Week 4	

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	87	43		
Units: Percentage Change				
least squares mean (confidence interval 95%)	33.02 (23.44 to 42.6)	6.73 (-5.27 to 18.73)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description: Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	26.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.99
upper limit	38.58

Secondary: Percentage Change From Baseline in Lathosterol at Week 8

End point title	Percentage Change From Baseline in Lathosterol at Week 8
-----------------	--

End point description:

Plasma lathosterol measured at baseline and after 8 weeks of study drug administration.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline and Week 8

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	86	44		
Units: Percentage Change				
least squares mean (confidence interval 95%)	35.87 (26.14 to 45.61)	-0.82 (-12.99 to 11.34)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
----------------------------	---

Statistical analysis description:

Analysis performed using an ANCOVA mixed model with fixed effects for treatment, baseline covariate corresponding to the analysis parameter, gender, primary diagnosis, study week and treatment by study week interaction.

Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Mean
Point estimate	36.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	24.12
upper limit	49.28

Secondary: Percentage Change From Baseline in Lathosterol at Week 12

End point title	Percentage Change From Baseline in Lathosterol at Week 12
-----------------	---

End point description:

Plasma lathosterol measured at baseline and after 12 weeks of study drug administration.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline and Week 12

End point values	Ezetimibe 10 mg - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	82	41		
Units: Percentage Change				
least squares mean (confidence interval 95%)	36.62 (26.46 to 46.78)	12.57 (-0.36 to 25.5)		

Statistical analyses

Statistical analysis title	Comparison of Percentage Change from Baseline
Statistical analysis description:	
Analysis performed using an ANCOVA mixed model with fixed effects for baseline covariate corresponding to the analysis parameter, treatment, gender, primary diagnosis (HeFH, Non-familial), study week (2, 4, 8, 12), and treatment by study week interaction.	
Comparison groups	Ezetimibe 10 mg - Efficacy v Placebo - Efficacy
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in Least-Squares Means
Point estimate	24.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.43
upper limit	37.67

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 12 weeks

Adverse event reporting additional description:

All-Patients-as-Treated (APaT) Population defined as all randomized participants who received at least one dose of double-blind study therapy.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	15.0
--------------------	------

Reporting groups

Reporting group title	Placebo
-----------------------	---------

Reporting group description: -

Reporting group title	Ezetimibe 10 mg
-----------------------	-----------------

Reporting group description: -

Serious adverse events	Placebo	Ezetimibe 10 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 45 (0.00%)	2 / 92 (2.17%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Congenital, familial and genetic disorders			
Epilepsy Congenital			
subjects affected / exposed	0 / 45 (0.00%)	1 / 92 (1.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 92 (1.09%)	
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	Ezetimibe 10 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 45 (40.00%)	27 / 92 (29.35%)	
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 45 (13.33%)	4 / 92 (4.35%)	
occurrences (all)	6	9	
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	5 / 45 (11.11%)	4 / 92 (4.35%)	
occurrences (all)	6	4	
Diarrhoea			
subjects affected / exposed	4 / 45 (8.89%)	1 / 92 (1.09%)	
occurrences (all)	5	2	
Nausea			
subjects affected / exposed	3 / 45 (6.67%)	1 / 92 (1.09%)	
occurrences (all)	3	1	
Vomiting			
subjects affected / exposed	3 / 45 (6.67%)	2 / 92 (2.17%)	
occurrences (all)	3	2	
Infections and infestations			
Influenza			
subjects affected / exposed	3 / 45 (6.67%)	5 / 92 (5.43%)	
occurrences (all)	3	5	
Nasopharyngitis			
subjects affected / exposed	5 / 45 (11.11%)	10 / 92 (10.87%)	
occurrences (all)	5	10	
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 45 (2.22%)	7 / 92 (7.61%)	
occurrences (all)	1	7	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported