



Clinical trial results:

A Placebo-Controlled, Double-Blind, Randomized Phase 2 Study to Evaluate the Effect of Obicetrapib in Combination with Ezetimibe in Participants with Mild Dyslipidemia

Summary

EudraCT number	2019-004935-22
Trial protocol	NL
Global end of trial date	30 June 2021

Results information

Result version number	v1 (current)
This version publication date	22 September 2024
First version publication date	22 September 2024

Trial information

Trial identification

Sponsor protocol code	TA-8995-303
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04770389
WHO universal trial number (UTN)	-
Other trial identifiers	Nickname:: OCEAN

Notes:

Sponsors

Sponsor organisation name	NewAmsterdam Pharma BV
Sponsor organisation address	Gooimeer 2-35 , DC Naarden , Netherlands, 1411
Public contact	Study Director, NewAmsterdam Pharma BV, +31 352062971, study.director@newamsterdampharma.com
Scientific contact	Study Director, NewAmsterdam Pharma BV, +31 352062971, study.director@newamsterdampharma.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	12 November 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 May 2021
Global end of trial reached?	Yes
Global end of trial date	30 June 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the effect of obicetrapib in combination with ezetimibe compared to placebo on low-density lipoprotein cholesterol (LDL-C) at Day 57.

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki and with all applicable laws and regulations of the locale and country where the study was conducted, and in compliance with Good Clinical Practice Guidelines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 October 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

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

Country: Number of subjects enrolled	Netherlands: 95
Country: Number of subjects enrolled	United States: 17
Worldwide total number of subjects	112
EEA total number of subjects	95

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)	90
From 65 to 84 years	22
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

112 participants were randomized. One participant in the ezetimibe monotherapy 10 mg group was randomized in error and did not participate in the study or receive study drug.

Pre-assignment

Screening details:

234 participants were screened

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Matching placebo tablet (ezetimibe)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

once daily matching placebo tablet (ezetimibe)

Investigational medicinal product name	Matching placebo tablet (obicetrapib)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Once daily matching placebo tablet (obicetrapib)

Arm title	Combination Therapy
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Arm description:

5 mg obicetrapib + 10 mg ezetimibe; once daily

Arm type	Experimental
Investigational medicinal product name	Obicetrapib 5 mg tablet
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

once daily 5 mg obicetrapib tablet

Investigational medicinal product name	Ezetimibe 10 mg tablet
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet

Routes of administration	Oral use
Dosage and administration details: once daily 10 mg ezetimibe tablet	
Arm title	Obicetrapib Monotherapy
Arm description: 5 mg obicetrapib + placebo ezetimibe; once daily	
Arm type	Experimental
Investigational medicinal product name	Obicetrapib 5 mg tablet
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: once daily 5 mg obicetrapib tablet	
Investigational medicinal product name	Matching placebo tablet (ezetimibe)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: once daily matching placebo tablet (ezetimibe)	
Arm title	Ezetimibe Monotherapy
Arm description: placebo obicetrapib + 10 mg ezetimibe; once daily	
Arm type	Experimental
Investigational medicinal product name	Ezetimibe 10 mg tablet
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: once daily 10 mg ezetimibe tablet	
Investigational medicinal product name	Matching placebo tablet (obicetrapib)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Once daily matching placebo tablet (obicetrapib)	

Number of subjects in period 1^[1]	Placebo	Combination Therapy	Obicetrapib Monotherapy
Started	28	27	28
Completed	26	22	26
Not completed	2	5	2
Left the country	-	-	1
Consent withdrawn by subject	-	2	-
Adverse event, non-fatal	1	2	1
Moved away from study site	-	1	-
Lost to follow-up	-	-	-
Failed attempt to draw blood	1	-	-

Number of subjects in period 1^[1]	Ezetimibe Monotherapy
Started	28
Completed	24
Not completed	4
Left the country	2
Consent withdrawn by subject	-
Adverse event, non-fatal	1
Moved away from study site	-
Lost to follow-up	1
Failed attempt to draw blood	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Baseline Population is defined as all participants who received at least one dose of study drug and had a baseline value for LDL-C assessment. One participant in the ezetimibe monotherapy (10 mg) group was randomized in error and did not participate in the study or receive study drug

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Combination Therapy
Reporting group description: 5 mg obicetrapib + 10 mg ezetimibe; once daily	
Reporting group title	Obicetrapib Monotherapy
Reporting group description: 5 mg obicetrapib + placebo ezetimibe; once daily	
Reporting group title	Ezetimibe Monotherapy
Reporting group description: placebo obicetrapib + 10 mg ezetimibe; once daily	

Reporting group values	Placebo	Combination Therapy	Obicetrapib Monotherapy
Number of subjects	28	27	28
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean standard deviation	54.5 ± 9.81	53.5 ± 11.43	59.1 ± 7.50
Gender categorical Units: Subjects			
Female	16	16	14
Male	12	11	14
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	26	26	27
Unknown or Not Reported	2	1	1
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	3	5	4
Native Hawaiian or Other Pacific Islander	0	0	0

Black or African American	1	0	1
White	24	22	23
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Baseline Low-Density Lipoprotein Cholesterol (LDL-C) Values			
Baseline LDL-C is defined as the last measurement prior to the first dose of study drug. LDL-C was calculated using the Friedewald Formula.			
Units: milligram per deciliter (mg/dL)			
arithmetic mean	136.8	132.2	127.5
standard deviation	± 19.86	± 27.48	± 20.87

Reporting group values	Ezetimibe Monotherapy	Total	
Number of subjects	28	111	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Units: years			
arithmetic mean	54.4		
standard deviation	± 9.55	-	
Gender categorical			
Units: Subjects			
Female	14	60	
Male	14	51	
Ethnicity			
Units: Subjects			
Hispanic or Latino	1	1	
Not Hispanic or Latino	25	104	
Unknown or Not Reported	2	6	
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	4	16	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	2	
White	24	93	
More than one race	0	0	
Unknown or Not Reported	0	0	

Baseline Low-Density Lipoprotein Cholesterol (LDL-C) Values			
Baseline LDL-C is defined as the last measurement prior to the first dose of study drug. LDL-C was calculated using the Friedewald Formula.			
Units: milligram per deciliter (mg/dL)			
arithmetic mean	120.0		
standard deviation	± 22.33	-	

Subject analysis sets

Subject analysis set title	Baseline Population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The study was revised from a 12-week treatment period to an 8-week treatment period in response to the global COVID-19 pandemic. The Baseline Population is defined as all participants who received at least one dose of study drug and had a baseline value for LDL-C assessment.

Reporting group values	Baseline Population		
Number of subjects	111		
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
arithmetic mean	55.4		
standard deviation	± 9.78		
Gender categorical			
Units: Subjects			
Female	60		
Male	51		
Ethnicity			
Units: Subjects			
Hispanic or Latino	1		
Not Hispanic or Latino	104		
Unknown or Not Reported	6		
Race			
Units: Subjects			
American Indian or Alaska Native	0		
Asian	16		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	2		
White	93		

More than one race	0		
Unknown or Not Reported	0		

Baseline Low-Density Lipoprotein Cholesterol (LDL-C) Values			
Baseline LDL-C is defined as the last measurement prior to the first dose of study drug. LDL-C was calculated using the Friedewald Formula.			
Units: milligram per deciliter (mg/dL)			
arithmetic mean	131.13		
standard deviation	± 22.64		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	-
Reporting group title	Combination Therapy
Reporting group description:	5 mg obicetrapib + 10 mg ezetimibe; once daily
Reporting group title	Obicetrapib Monotherapy
Reporting group description:	5 mg obicetrapib + placebo ezetimibe; once daily
Reporting group title	Ezetimibe Monotherapy
Reporting group description:	placebo obicetrapib + 10 mg ezetimibe; once daily
Subject analysis set title	Baseline Population
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	The study was revised from a 12-week treatment period to an 8-week treatment period in response to the global COVID-19 pandemic. The Baseline Population is defined as all participants who received at least one dose of study drug and had a baseline value for LDL-C assessment.

Primary: 1. Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Placebo [Friedewald] [Time Frame: 8 weeks]

End point title	1. Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Placebo [Friedewald] [Time Frame: 8 weeks] ^[1]
End point description:	Mean percent change in LDL-C from baseline to Day 57; LDL-C determined using the Friedewald formula
End point type	Primary
End point timeframe:	8 weeks
Notes:	[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The end point only includes a comparison of 2 arms

End point values	Placebo	Combination Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	24		
Units: Percent Change from Baseline				
arithmetic mean (standard deviation)	-0.17 (± 12.682)	-45.63 (± 21.677)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Combination Therapy v Placebo

Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[2]
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) Mean
Point estimate	-44.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-55.2
upper limit	-34.63
Variability estimate	Standard error of the mean
Dispersion value	5.183

Notes:

[2] - mixed model for repeated measures (MMRM) with missing at random assumption

Primary: 2. Median Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Placebo [Friedewald] [Time Frame: 8 weeks]

End point title	2. Median Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Placebo [Friedewald] [Time Frame: 8 weeks] ^[3]
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End point description:

Median percent change in LDL-C from baseline to Day 57; LDL-C determined using the Friedewald formula

End point type	Primary
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End point timeframe:

8 weeks

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point only includes a comparison of 2 arms

End point values	Placebo	Combination Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	24		
Units: Percent Change from Baseline				
median (full range (min-max))	-1.40 (-20.9 to 33.6)	-51.95 (-77.9 to 3.1)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Combination Therapy

Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[4]
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) Mean
Point estimate	-44.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-55.2
upper limit	-34.63
Variability estimate	Standard error of the mean
Dispersion value	5.183

Notes:

[4] - mixed model for repeated measures (MMRM) with missing at random assumption

Primary: 3. LS Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Placebo [Friedewald] [Time Frame: 8 weeks]

End point title	3. LS Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Placebo [Friedewald] [Time Frame: 8 weeks] ^[5]
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End point description:

LS Mean percent change in LDL-C from baseline to Day 57; LDL-C determined using the Friedewald formula

End point type	Primary
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End point timeframe:

8 weeks

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The end point only includes a comparison of 2 arms

End point values	Placebo	Combination Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	27		
Units: Percent Change from Baseline				
least squares mean (standard error)	1.37 (± 3.604)	-43.55 (± 3.746)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Combination Therapy

Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[6]
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) Mean
Point estimate	-44.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-55.2
upper limit	-34.63
Variability estimate	Standard error of the mean
Dispersion value	5.183

Notes:

[6] - mixed model for repeated measures (MMRM) with missing at random assumption

Primary: 4. Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Placebo [PUC]

End point title	4. Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Placebo [PUC] ^[7]
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End point description:

Mean percent change in LDL-C from baseline to Day 57; LDL-C measured using preparative ultracentrifugation (PUC)

End point type	Primary
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End point timeframe:

8 weeks

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The end point only includes a comparison of 2 arms

End point values	Placebo	Combination Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	24		
Units: Percent Change from Baseline				
arithmetic mean (standard deviation)	-1.53 (± 15.105)	-44.38 (± 20.731)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Combination Therapy

Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Least Squares (LS) Mean
Point estimate	-43.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-54.29
upper limit	-32.36
Variability estimate	Standard error of the mean
Dispersion value	5.517

Primary: 5. Median Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Placebo [PUC]

End point title	5. Median Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Placebo [PUC] ^[8]
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End point description:

Median percent change in LDL-C from baseline to Day 57; LDL-C measured using preparative ultracentrifugation (PUC)

End point type	Primary
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End point timeframe:

8 weeks

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The end point only includes a comparison of 2 arms

End point values	Placebo	Combination Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	24		
Units: Percent Change from Baseline				
median (full range (min-max))	-2.00 (-24.5 to 35.9)	-51.40 (-69.6 to 8.1)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Combination Therapy

Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Least Squares (LS) Mean
Point estimate	-43.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-54.29
upper limit	-32.36
Variability estimate	Standard error of the mean
Dispersion value	5.517

Primary: 6. LS Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Placebo [PUC]

End point title	6. LS Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Placebo [PUC] ^[9]
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End point description:

LS Mean percent change in LDL-C from baseline to Day 57; LDL-C measured using preparative ultracentrifugation (PUC)

End point type	Primary
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End point timeframe:

8 weeks

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The end point only includes a comparison of 2 arms

End point values	Placebo	Combination Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	24		
Units: Percent Change from Baseline				
least squares mean (standard error)	-0.78 (± 4.012)	-44.10 (± 3.813)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Combination Therapy

Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Least Squares (LS) Mean
Point estimate	-43.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-54.29
upper limit	-32.36
Variability estimate	Standard error of the mean
Dispersion value	5.517

Secondary: 7. Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib Monotherapy Compared to Placebo [Friedewald]

End point title	7. Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib Monotherapy Compared to Placebo [Friedewald] ^[10]
End point description:	Mean percent change in LDL-C from baseline to Day 57; LDL-C determined using the Friedewald formula
End point type	Secondary
End point timeframe:	8 weeks
Notes:	[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The end point only includes a comparison of 2 arms

End point values	Placebo	Obicetrapib Monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	25		
Units: Percent Change from Baseline				
arithmetic mean (standard deviation)	-0.17 (± 12.682)	-31.88 (± 18.860)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Obicetrapib Monotherapy v Placebo

Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) Mean
Point estimate	-33.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-43.63
upper limit	-23.09
Variability estimate	Standard error of the mean
Dispersion value	5.176

Secondary: 8. Median Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib Monotherapy Compared to Placebo [Friedewald]

End point title	8. Median Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib Monotherapy Compared to Placebo [Friedewald] ^[11]
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End point description:

Median percent change in LDL-C from baseline to Day 57; LDL-C determined using the Friedewald formula

End point type	Secondary
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End point timeframe:

8 weeks

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The end point only includes a comparison of 2 arms

End point values	Placebo	Obicetrapib Monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	25		
Units: Percent Change from Baseline				
median (full range (min-max))	-1.40 (-20.9 to 33.6)	-34.40 (-57.0 to 23.8)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Obicetrapib Monotherapy

Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) Mean
Point estimate	-33.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-43.63
upper limit	-23.09
Variability estimate	Standard error of the mean
Dispersion value	5.176

Secondary: 9. LS Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib Monotherapy Compared to Placebo [Friedewald]

End point title	9. LS Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib Monotherapy Compared to Placebo [Friedewald] ^[12]
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End point description:

LS Mean percent change in LDL-C from baseline to Day 57; LDL-C determined using the Friedewald formula

End point type	Secondary
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End point timeframe:

8 weeks

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The end point only includes a comparison of 2 arms

End point values	Placebo	Obicetrapib Monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	28		
Units: Percent Change from Baseline				
least squares mean (standard error)	1.37 (± 3.604)	-31.99 (± 3.686)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Obicetrapib Monotherapy

Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) Mean
Point estimate	-33.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-43.63
upper limit	-23.09
Variability estimate	Standard error of the mean
Dispersion value	5.176

Secondary: 10. Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib Monotherapy Compared to Placebo [PUC]

End point title	10. Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib Monotherapy Compared to Placebo [PUC] ^[13]
End point description:	Mean percent change in LDL-C from baseline to Day 57; LDL-C measured using preparative ultracentrifugation (PUC)
End point type	Secondary
End point timeframe:	8 weeks

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The end point only includes a comparison of 2 arms

End point values	Placebo	Obicetrapib Monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	25		
Units: Percent Change from Baseline				
arithmetic mean (standard deviation)	-1.53 (± 15.105)	-27.94 (± 18.914)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Obicetrapib Monotherapy

Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Least Squares (LS) Mean
Point estimate	-28.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-39.32
upper limit	-17.08
Variability estimate	Standard error of the mean
Dispersion value	5.596

Secondary: 11. Median Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib Monotherapy Compared to Placebo [PUC]

End point title	11. Median Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib Monotherapy Compared to Placebo [PUC] ^[14]
End point description:	Median percent change in LDL-C from baseline to Day 57; LDL-C measured using preparative ultracentrifugation (PUC)
End point type	Secondary
End point timeframe:	8 weeks

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The end point only includes a comparison of 2 arms

End point values	Placebo	Obicetrapib Monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	25		
Units: Percent Change from Baseline				
median (full range (min-max))	-2.00 (-24.5 to 35.9)	-30.10 (-56.7 to 19.1)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Obicetrapib Monotherapy

Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Least Squares (LS) Mean
Point estimate	-28.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-39.32
upper limit	-17.08
Variability estimate	Standard error of the mean
Dispersion value	5.596

Secondary: 12. LS Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib Monotherapy Compared to Placebo [PUC]

End point title	12. LS Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib Monotherapy Compared to Placebo [PUC] ^[15]
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End point description:

LS Mean percent change in LDL-C from baseline to Day 57; LDL-C measured using preparative ultracentrifugation (PUC)

End point type	Secondary
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End point timeframe:

8 weeks

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The end point only includes a comparison of 2 arms

End point values	Placebo	Obicetrapib Monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	25		
Units: Percent Change from Baseline				
least squares mean (standard error)	-0.78 (± 4.012)	-28.98 (± 3.802)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Obicetrapib Monotherapy

Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Least Squares (LS) Mean
Point estimate	-28.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-39.32
upper limit	-17.08
Variability estimate	Standard error of the mean
Dispersion value	5.596

Secondary: 13. Mean Percent Change in Apolipoprotein-B (ApoB) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Placebo

End point title	13. Mean Percent Change in Apolipoprotein-B (ApoB) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Placebo ^[16]
End point description:	
Mean percent change in ApoB from baseline to Day 57	
End point type	Secondary
End point timeframe:	
8 weeks	

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The end point only includes a comparison of 2 arms

End point values	Placebo	Combination Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	24		
Units: Percent Change from Baseline				
arithmetic mean (standard deviation)	-1.17 (± 11.692)	-31.62 (± 15.521)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Combination Therapy v Placebo

Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) Mean
Point estimate	-29.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-37.12
upper limit	-22.12
Variability estimate	Standard error of the mean
Dispersion value	3.78

Secondary: 14. Median Percent Change in Apolipoprotein-B (ApoB) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Placebo

End point title	14. Median Percent Change in Apolipoprotein-B (ApoB) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Placebo ^[17]
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End point description:

Median percent change in ApoB from baseline to Day 57

End point type	Secondary
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End point timeframe:

8 weeks

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The end point only includes a comparison of 2 arms

End point values	Placebo	Combination Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	24		
Units: Percent Change from Baseline				
median (full range (min-max))	-0.90 (-19.8 to 25.4)	-34.75 (-53.0 to 8.9)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Combination Therapy

Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) Mean
Point estimate	-29.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-37.12
upper limit	-22.12
Variability estimate	Standard error of the mean
Dispersion value	3.78

Secondary: 15. LS Mean Percent Change in Apolipoprotein-B (ApoB) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Placebo

End point title	15. LS Mean Percent Change in Apolipoprotein-B (ApoB) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Placebo ^[18]
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End point description:

LS Mean percent change in ApoB from baseline to Day 57

End point type	Secondary
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End point timeframe:

8 weeks

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The end point only includes a comparison of 2 arms

End point values	Placebo	Combination Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	27		
Units: Percent Change from Baseline				
least squares mean (standard error)	-0.11 (± 2.626)	-29.73 (± 2.730)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Combination Therapy

Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) Mean
Point estimate	-29.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-37.12
upper limit	-22.12
Variability estimate	Standard error of the mean
Dispersion value	3.78

Secondary: 16. Mean Percent Change in Apolipoprotein-B (ApoB) From Baseline to Day 57: Obicetrapib Monotherapy Compared to Placebo

End point title	16. Mean Percent Change in Apolipoprotein-B (ApoB) From Baseline to Day 57: Obicetrapib Monotherapy Compared to Placebo ^[19]
End point description:	
Mean percent change in Apo-B from baseline to Day 57	
End point type	Secondary
End point timeframe:	
8 weeks	

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The end point only includes a comparison of 2 arms

End point values	Placebo	Obicetrapib Monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Percent Change from Baseline				
arithmetic mean (standard deviation)	-1.17 (± 11.692)	-22.15 (± 13.356)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Obicetrapib Monotherapy

Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) Mean
Point estimate	-22.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.83
upper limit	-14.88
Variability estimate	Standard error of the mean
Dispersion value	3.768

Secondary: 17. Median Percent Change in Apolipoprotein-B (ApoB) From Baseline to Day 57: Obicetrapib Monotherapy Compared to Placebo

End point title	17. Median Percent Change in Apolipoprotein-B (ApoB) From Baseline to Day 57: Obicetrapib Monotherapy Compared to Placebo ^[20]
End point description:	
Median percent change in Apo-B from baseline to Day 57	
End point type	Secondary
End point timeframe:	
8 weeks	

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The end point only includes a comparison of 2 arms

End point values	Placebo	Obicetrapib Monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Percent Change from Baseline				
median (full range (min-max))	-0.90 (-19.8 to 25.4)	-23.50 (-39.3 to 21.2)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Obicetrapib Monotherapy

Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) Mean
Point estimate	-22.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.83
upper limit	-14.88
Variability estimate	Standard error of the mean
Dispersion value	3.768

Secondary: 18. LS Mean Percent Change in Apolipoprotein-B (ApoB) From Baseline to Day 57: Obicetrapib Monotherapy Compared to Placebo

End point title	18. LS Mean Percent Change in Apolipoprotein-B (ApoB) From Baseline to Day 57: Obicetrapib Monotherapy Compared to Placebo ^[21]
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End point description:

LS Mean percent change in Apo-B from baseline to Day 57

End point type	Secondary
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End point timeframe:

8 weeks

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The end point only includes a comparison of 2 arms

End point values	Placebo	Obicetrapib Monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	28		
Units: Percent Change from Baseline				
least squares mean (standard error)	-0.11 (± 2.626)	-22.46 (± 2.675)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Obicetrapib Monotherapy

Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) Mean
Point estimate	-22.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.83
upper limit	-14.88
Variability estimate	Standard error of the mean
Dispersion value	3.768

Secondary: 19. Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Ezetimibe Monotherapy [Friedewald]

End point title	19. Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Ezetimibe Monotherapy [Friedewald] ^[22]
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End point description:

Mean percent change in LDL-C from baseline to Day 57; LDL-C determined using the Friedewald formula

End point type	Secondary
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End point timeframe:

8 weeks

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The end point only includes a comparison of 2 arms

End point values	Combination Therapy	Ezetimibe Monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: Percent Change from Baseline				
arithmetic mean (standard deviation)	-45.63 (± 21.677)	-12.69 (± 21.316)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Combination Therapy v Ezetimibe Monotherapy

Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) Mean
Point estimate	-30.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-40.55
upper limit	-19.71
Variability estimate	Standard error of the mean
Dispersion value	5.254

Secondary: 20. Median Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Ezetimibe Monotherapy [Friedewald]

End point title	20. Median Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Ezetimibe Monotherapy [Friedewald] ^[23]
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End point description:

Median percent change in LDL-C from baseline to Day 57; LDL-C determined using the Friedewald formula

End point type	Secondary
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End point timeframe:

8 weeks

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The end point only includes a comparison of 2 arms

End point values	Combination Therapy	Ezetimibe Monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: Percent Change from Baseline				
median (full range (min-max))	-51.95 (-77.9 to 3.1)	-14.80 (-51.9 to 59.1)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Combination Therapy v Ezetimibe Monotherapy

Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) Mean
Point estimate	-30.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-40.55
upper limit	-19.71
Variability estimate	Standard error of the mean
Dispersion value	5.254

Secondary: 21. LS Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Ezetimibe Monotherapy [Friedewald]

End point title	21. LS Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Ezetimibe Monotherapy [Friedewald] ^[24]
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End point description:

LS Mean percent change in LDL-C from baseline to Day 57; LDL-C determined using the Friedewald formula

End point type	Secondary
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End point timeframe:

8 weeks

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The end point only includes a comparison of 2 arms

End point values	Combination Therapy	Ezetimibe Monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	28		
Units: Percent Change from Baseline				
least squares mean (standard error)	-43.55 (± 3.746)	-13.42 (± 3.675)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Combination Therapy v Ezetimibe Monotherapy

Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) Mean
Point estimate	-30.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-40.55
upper limit	-19.71
Variability estimate	Standard error of the mean
Dispersion value	5.254

Secondary: 22. Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib Monotherapy Compared to Ezetimibe Monotherapy [Friedewald]

End point title	22. Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib Monotherapy Compared to Ezetimibe Monotherapy [Friedewald] ^[25]
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End point description:

Mean percent change in LDL-C from baseline to Day 57; LDL-C determined using the Friedewald formula

End point type	Secondary
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End point timeframe:

8 weeks

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The end point only includes a comparison of 2 arms

End point values	Obicetrapib Monotherapy	Ezetimibe Monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	25		
Units: Percent Change from Baseline				
arithmetic mean (standard deviation)	-31.88 (± 18.860)	-12.69 (± 21.316)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Obicetrapib Monotherapy v Ezetimibe Monotherapy

Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) Mean
Point estimate	-18.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.88
upper limit	-8.27
Variability estimate	Standard error of the mean
Dispersion value	5.196

Secondary: 23. Median Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib Monotherapy Compared to Ezetimibe Monotherapy [Friedewald]

End point title	23. Median Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib Monotherapy Compared to Ezetimibe Monotherapy [Friedewald] ^[26]
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End point description:

Median percent change in LDL-C from baseline to Day 57; LDL-C determined using the Friedewald formula

End point type	Secondary
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End point timeframe:

8 weeks

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The end point only includes a comparison of 2 arms

End point values	Obicetrapib Monotherapy	Ezetimibe Monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	25		
Units: Percent Change from Baseline				
median (full range (min-max))	-34.40 (-57.0 to 23.8)	-14.80 (-51.9 to 59.1)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Obicetrapib Monotherapy v Ezetimibe Monotherapy

Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) Mean
Point estimate	-18.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.88
upper limit	-8.27
Variability estimate	Standard error of the mean
Dispersion value	5.196

Secondary: 24. LS Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib Monotherapy Compared to Ezetimibe Monotherapy [Friedewald]

End point title	24. LS Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Obicetrapib Monotherapy Compared to Ezetimibe Monotherapy [Friedewald] ^[27]
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End point description:

LS Mean percent change in LDL-C from baseline to Day 57; LDL-C calculated using the Friedewald formula

End point type	Secondary
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End point timeframe:

8 weeks

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The end point only includes a comparison of 2 arms

End point values	Obicetrapib Monotherapy	Ezetimibe Monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	28		
Units: Percent Change from Baseline				
least squares mean (standard error)	-31.99 (± 3.686)	-13.42 (± 3.675)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Obicetrapib Monotherapy v Ezetimibe Monotherapy

Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0005
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) Mean
Point estimate	-18.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.88
upper limit	-8.27
Variability estimate	Standard error of the mean
Dispersion value	5.196

Secondary: 25. Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Ezetimibe Monotherapy Compared to Placebo [Friedewald]

End point title	25. Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Ezetimibe Monotherapy Compared to Placebo [Friedewald] ^[28]
End point description:	Mean percent change in LDL-C from baseline to Day 57; LDL-C determined using the Friedewald formula
End point type	Secondary
End point timeframe:	8 weeks
Notes:	<p>[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.</p> <p>Justification: The end point only includes a comparison of 2 arms</p>

End point values	Placebo	Ezetimibe Monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	25		
Units: Percent Change from Baseline				
arithmetic mean (standard deviation)	-0.17 (± 12.682)	-12.69 (± 21.316)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Ezetimibe Monotherapy

Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0051
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) Mean
Point estimate	-14.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.03
upper limit	-4.54
Variability estimate	Standard error of the mean
Dispersion value	5.165

Secondary: 26. Median Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Ezetimibe Monotherapy Compared to Placebo [Friedewald]

End point title	26. Median Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Ezetimibe Monotherapy Compared to Placebo [Friedewald] ^[29]
End point description:	Median percent change in LDL-C from baseline to Day 57; LDL-C calculated using the Friedewald formula
End point type	Secondary
End point timeframe:	8 weeks
Notes:	<p>[29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.</p> <p>Justification: The end point only includes a comparison of 2 arms</p>

End point values	Placebo	Ezetimibe Monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	25		
Units: Percent Change from Baseline				
median (full range (min-max))	-1.40 (-20.9 to 33.6)	-14.80 (-51.9 to 59.1)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Ezetimibe Monotherapy

Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0051
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) Mean
Point estimate	-14.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.03
upper limit	-4.54
Variability estimate	Standard error of the mean
Dispersion value	5.165

Secondary: 27. LS Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Ezetimibe Monotherapy Compared to Placebo [Friedewald]

End point title	27. LS Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Ezetimibe Monotherapy Compared to Placebo [Friedewald] ^[30]
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End point description:

LS Mean percent change in LDL-C from baseline to Day 57; LDL-C calculated using the Friedewald formula

End point type	Secondary
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End point timeframe:

8 weeks

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The end point only includes a comparison of 2 arms

End point values	Placebo	Ezetimibe Monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	28		
Units: Percent Change from Baseline				
least squares mean (standard error)	1.37 (± 3.604)	-13.42 (± 3.675)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Ezetimibe Monotherapy

Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0051
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) Mean
Point estimate	-14.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.03
upper limit	-4.54
Variability estimate	Standard error of the mean
Dispersion value	5.165

Secondary: 28. Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Ezetimibe Monotherapy Compared to Placebo [PUC]

End point title	28. Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Ezetimibe Monotherapy Compared to Placebo [PUC] ^[31]
End point description:	Mean percent change in LDL-C from baseline to Day 57; LDL-C measured using preparative ultracentrifugation (PUC)
End point type	Secondary
End point timeframe:	8 weeks

Notes:

[31] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The end point only includes a comparison of 2 arms

End point values	Placebo	Ezetimibe Monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	23		
Units: Percent Change from Baseline				
arithmetic mean (standard deviation)	-1.53 (± 15.105)	-13.68 (± 19.573)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Ezetimibe Monotherapy

Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0245
Method	ANCOVA
Parameter estimate	Least Squares (LS) Mean
Point estimate	-12.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.86
upper limit	-1.68
Variability estimate	Standard error of the mean
Dispersion value	5.58

Secondary: 29. Median Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Ezetimibe Monotherapy Compared to Placebo [PUC]

End point title	29. Median Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Ezetimibe Monotherapy Compared to Placebo [PUC] ^[32]
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End point description:

Median percent change in LDL-C from baseline to Day 57; LDL-C measured using preparative ultracentrifugation (PUC)

End point type	Secondary
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End point timeframe:

8 weeks

Notes:

[32] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The end point only includes a comparison of 2 arms

End point values	Placebo	Ezetimibe Monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	23		
Units: Percent Change from Baseline				
median (full range (min-max))	-2.00 (-24.5 to 35.9)	-14.90 (-46.8 to 46.9)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Ezetimibe Monotherapy

Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0245
Method	ANCOVA
Parameter estimate	Least Squares (LS) Mean
Point estimate	-12.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.86
upper limit	-1.68
Variability estimate	Standard error of the mean
Dispersion value	5.58

Secondary: 30. LS Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Ezetimibe Monotherapy Compared to Placebo [PUC]

End point title	30. LS Mean Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 57: Ezetimibe Monotherapy Compared to Placebo [PUC] ^[33]
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End point description:

LS Mean percent change in LDL-C from baseline to Day 57; LDL-C measured using preparative ultracentrifugation (PUC)

End point type	Secondary
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End point timeframe:

8 weeks

Notes:

[33] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The end point only includes a comparison of 2 arms

End point values	Placebo	Ezetimibe Monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	23		
Units: Percent Change from Baseline				
least squares mean (standard error)	-0.78 (± 4.012)	-13.55 (± 3.891)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Ezetimibe Monotherapy

Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0245
Method	ANCOVA
Parameter estimate	Least Squares (LS) Mean
Point estimate	-12.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.86
upper limit	-1.68
Variability estimate	Standard error of the mean
Dispersion value	5.58

Secondary: 31. Mean Percent Change in Apolipoprotein-B (ApoB) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Ezetimibe Monotherapy

End point title	31. Mean Percent Change in Apolipoprotein-B (ApoB) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Ezetimibe Monotherapy ^[34]
End point description:	
Mean percent change in ApoB from baseline to Day 57	
End point type	Secondary
End point timeframe:	
8 weeks	
Notes:	
[34] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.	
Justification: The end point only includes a comparison of 2 arms	

End point values	Combination Therapy	Ezetimibe Monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: Percent Change from Baseline				
arithmetic mean (standard deviation)	-31.62 (± 15.521)	-8.78 (± 14.445)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Combination Therapy v Ezetimibe Monotherapy

Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) Mean
Point estimate	-20.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.39
upper limit	-13.22
Variability estimate	Standard error of the mean
Dispersion value	3.822

Secondary: 32. Median Percent Change in Apolipoprotein-B (ApoB) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Ezetimibe Monotherapy

End point title	32. Median Percent Change in Apolipoprotein-B (ApoB) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Ezetimibe Monotherapy ^[35]
End point description:	
Median percent change in ApoB from baseline to Day 57	
End point type	Secondary
End point timeframe:	
8 weeks	
Notes:	
[35] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.	
Justification: The end point only includes a comparison of 2 arms	

End point values	Combination Therapy	Ezetimibe Monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: Percent Change from Baseline				
median (full range (min-max))	-34.75 (-53.0 to 8.9)	-8.90 (-45.4 to 32.3)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Combination Therapy v Ezetimibe Monotherapy

Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) Mean
Point estimate	-20.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.39
upper limit	-13.22
Variability estimate	Standard error of the mean
Dispersion value	3.822

Secondary: 33. LS Mean Percent Change in Apolipoprotein-B (ApoB) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Ezetimibe Monotherapy

End point title	33. LS Mean Percent Change in Apolipoprotein-B (ApoB) From Baseline to Day 57: Obicetrapib in Combination With Ezetimibe Compared to Ezetimibe Monotherapy ^[36]
End point description:	LS Mean Percent change in ApoB from baseline to Day 57
End point type	Secondary
End point timeframe:	8 weeks
Notes:	<p>[36] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.</p> <p>Justification: The end point only includes a comparison of 2 arms</p>

End point values	Combination Therapy	Ezetimibe Monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	28		
Units: Percent Change from Baseline				
least squares mean (standard error)	-29.73 (± 2.730)	-8.92 (± 2.675)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Combination Therapy v Ezetimibe Monotherapy

Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) Mean
Point estimate	-20.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.39
upper limit	-13.22
Variability estimate	Standard error of the mean
Dispersion value	3.822

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug through Week 16

Adverse event reporting additional description:

Safety Population included all participants who received at least 1 dose of any study drug.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.0
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Reporting groups

Reporting group title	Placebo
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Reporting group description: -

Reporting group title	Combination Therapy
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Reporting group description:

5 mg obicetrapib + 10 mg ezetimibe; once daily

Reporting group title	Obicetrapib Monotherapy
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Reporting group description:

5 mg obicetrapib + placebo ezetimibe; once daily

Reporting group title	Ezetimibe Monotherapy
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Reporting group description:

placebo obicetrapib + 10 mg ezetimibe; once daily

Serious adverse events	Placebo	Combination Therapy	Obicetrapib Monotherapy
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 28 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Multiple fractures			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Hyperventilation			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Ezetimibe Monotherapy		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 28 (7.14%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Multiple fractures			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Hyperventilation			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	Combination Therapy	Obicetrapib Monotherapy
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 28 (21.43%)	9 / 27 (33.33%)	4 / 28 (14.29%)
Investigations			
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			

subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 2	1 / 27 (3.70%) 1	0 / 28 (0.00%) 0
Dizziness subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 27 (3.70%) 2	0 / 28 (0.00%) 0
Sciatica subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	0 / 27 (0.00%) 0	0 / 28 (0.00%) 0
General disorders and administration site conditions Non-cardiac chest pain subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	0 / 27 (0.00%) 0	0 / 28 (0.00%) 0
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	2 / 27 (7.41%) 3	0 / 28 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	0 / 27 (0.00%) 0	0 / 28 (0.00%) 0
Abdominal pain subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 27 (3.70%) 1	0 / 28 (0.00%) 0
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	0 / 27 (0.00%) 0	0 / 28 (0.00%) 0
Flatulence subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 27 (0.00%) 0	1 / 28 (3.57%) 1
Respiratory, thoracic and mediastinal disorders Productive cough subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	0 / 27 (0.00%) 0	0 / 28 (0.00%) 0
Skin and subcutaneous tissue disorders Nail fold inflammation subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 27 (0.00%) 0	0 / 28 (0.00%) 0

Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Bursitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Temporomandibular joint syndrome			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	1 / 28 (3.57%)
occurrences (all)	0	1	1
COVID-19			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Onychomycosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	0 / 28 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Ezetimibe Monotherapy		
Total subjects affected by non-serious adverse events			

subjects affected / exposed	8 / 28 (28.57%)		
Investigations			
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Dizziness			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Sciatica			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Constipation			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			

subjects affected / exposed occurrences (all) Flatulence subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0 0 / 28 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Productive cough subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0		
Skin and subcutaneous tissue disorders Nail fold inflammation subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1		
Musculoskeletal and connective tissue disorders Myalgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Bursitis subjects affected / exposed occurrences (all) Temporomandibular joint syndrome subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1 0 / 28 (0.00%) 0 1 / 28 (3.57%) 1 0 / 28 (0.00%) 0		
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) COVID-19 subjects affected / exposed occurrences (all) Gastroenteritis subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0 0 / 28 (0.00%) 0 1 / 28 (3.57%) 1		

Influenza			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Onychomycosis			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 January 2021	<p>This amendment was written to address feedback from Competent Authorities and to mitigate the effects of the ongoing Coronavirus Disease 2019 (COVID-19) pandemic on the study's execution.</p> <p>Key changes to the protocol with rationale were as follows:</p> <ul style="list-style-type: none">• The sample size was reduced from approximately 152 participants to approximately 100 participants (25 per group).<ul style="list-style-type: none">o Rationale: To facilitate the completion of enrollment within an acceptable timeframe, whilst maintaining sufficient statistical power to address the scientific objectives of the study.• The geographical scope of the study was expanded to include the option for participation of sites in the USA.<ul style="list-style-type: none">o Rationale: To mitigate the effects of the ongoing COVID-19 pandemic on site operations, recruitment, and participant retention.• The Treatment Period was reduced from 12 weeks to 8 weeks.<ul style="list-style-type: none">o Rationale: To optimize participant retention and data completeness in the context of the COVID-19 pandemic, whilst maintaining the scientific integrity of the primary and secondary endpoints, which were still be evaluated at steady state for all study drugs.• The priority of some endpoints in the secondary endpoint hierarchy were revised.<ul style="list-style-type: none">o Rationale: To focus on key scientific questions raised by recent interactions with Competent Authorities.• The analysis of LDL-C has been amended so that this parameter will be calculated by the Friedewald formula, with preparative ultracentrifugation also used for evaluation for changes between baseline and end of treatment (the primary endpoint).<ul style="list-style-type: none">o Rationale: To optimize the analytical efficiency of the study, consistent with other studies in this indication. In addition, the lipid inclusion and exclusion criteria of the study and current scientific understanding about precision of the assessment of LDL-C levels by the Friedewald formula are such that an accurate assessment of the primary and key secondary endpoints can be guaranteed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported