Clinical trial results:
Obicetrapib on Top of Maximum Tolerated Lipid-Modifying Therapies (BROOKLYN): A Placebo-Controlled, Double-Blind, Randomized, Phase 3 Study to Evaluate the Effect of 10 mg Obicetrapib in Participants With a History of HeFH and LDL-C 70 mg/dL Who are Not Adequately Controlled by Their Lipid-Modifying Therapies

Summary

EudraCT number	2021-005064-22
Trial protocol	ES NL CZ PL
Global end of trial date	28 May 2024

Results information

Result version number	v1 (current)
This version publication date	12 June 2025
First version publication date	12 June 2025

Trial information

Trial identification

Sponsor protocol code	TA-8995-301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05425745
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	NewAmsterdam Pharma BV
Sponsor organisation address	Gooimeer 2-35, DC Naarden, Netherlands, 1411
Public contact	Study Director, NewAmsterdam Pharma B.V., +31 35 2062971 , study.director@newamsterdampharma.com
Scientific contact	Study Director, NewAmsterdam Pharma B.V., +31 35 2062971 , 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	04 December 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 May 2024
Global end of trial reached?	Yes
Global end of trial date	28 May 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the effect of obicetrapib on low-density lipoprotein cholesterol (LDL-C) levels at Day 84.

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	20 July 2022
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: 9
Country: Number of subjects enrolled	Norway: 9
Country: Number of subjects enrolled	Poland: 1
Country: Number of subjects enrolled	Spain: 50
Country: Number of subjects enrolled	Czechia: 45
Country: Number of subjects enrolled	United States: 57
Country: Number of subjects enrolled	South Africa: 58
Country: Number of subjects enrolled	Georgia: 88
Country: Number of subjects enrolled	Canada: 32
Country: Number of subjects enrolled	United Kingdom: 5
Worldwide total number of subjects	354
EEA total number of subjects	114

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)	254
From 65 to 84 years	99
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

513 patients were screened: out of 513, 354 participants were randomized: 236 participants to the obicetrapib 10 mg group and 118 participants to the placebo group

Pre-assignment

Screening details:

513 patients 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:

one placebo tablet once daily;
Placebo: placebo tablet made to resemble active

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

Dosage and administration details:

once daily matching placebo tablet

Arm title	Obicetrapib 10 mg

Arm description:

one 10 mg obicetrapib tablet once daily;
Obicetrapib: 10 mg obicetrapib tablet

Arm type	Experimental
Investigational medicinal product name	Obicetrapib 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 obicetrapib tablet

Number of subjects in period 1	Placebo	Obicetrapib 10 mg
Started	118	236
Completed	110	226
Not completed	8	10
Consent withdrawn by subject	3	3
End of study visit completed by phone	1	-
Subject decision	1	-
Adverse event, non-fatal	-	1
Death	2	3
Lost to follow-up	1	2
Did not return for end of study visit	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
one placebo tablet once daily; Placebo: placebo tablet made to resemble active	
Reporting group title	Obicetrapib 10 mg
Reporting group description:	
one 10 mg obicetrapib tablet once daily; Obicetrapib: 10 mg obicetrapib tablet	

Reporting group values	Placebo	Obicetrapib 10 mg	Total
Number of subjects	118	236	354
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	89	165	254
From 65-84 years	28	71	99
85 years and over	1	0	1
Age continuous Units: years			
arithmetic mean	56.6	57	
standard deviation	± 11.06	± 12.7	-
Gender categorical Units: Subjects			
Female	65	125	190
Male	53	111	164
Ethnicity Units: Subjects			
Hispanic or Latino	2	8	10
Not Hispanic or Latino	114	226	340
Unknown or Not Reported	2	2	4
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	6	7
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	3	3	6
White	110	219	329
More than one race	3	4	7
Unknown or Not Reported	1	4	5

Baseline Low-Density Lipoprotein Cholesterol (LDL-C)			
Measure Description: Baseline LDL-C is defined as the last measurement prior to the first dose of study drug. LDL-C was measured by Preparative Ultracentrifugation (PUC). Measure Analysis Population Description: 4 participants were missing baseline LDL-C (measured by PUC). 2 pts baseline LDL-C results were not available due to low volume or hemolysis. 2 pts were randomized but did not receive study drug. Therefore, baseline values (baseline defined as the last measurement prior to the first dose of study drug) were not available.			
Units: mg/dL			
arithmetic mean	119.9	123.4	
standard deviation	± 54.47	± 49.23	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
one placebo tablet once daily; Placebo: placebo tablet made to resemble active	
Reporting group title	Obicetrapib 10 mg
Reporting group description:	
one 10 mg obicetrapib tablet once daily; Obicetrapib: 10 mg obicetrapib tablet	

Primary: 1. Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 84 [PUC]

End point title	1. Percent Change in Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Day 84 [PUC]
End point description:	
LS mean percent change from baseline to Day 84 in Low-Density Lipoprotein Cholesterol (LDL-C) in the obicetrapib group compared to the placebo group [PUC]. LDL-C level was measured by preparative ultracentrifugation (PUC).	
End point type	Primary
End point timeframe:	
84 Days	

End point values	Placebo	Obicetrapib 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	232		
Units: Percent Change from Baseline				
least squares mean (standard error)	0.25 (± 2.480)	-36.05 (± 1.769)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Obicetrapib 10 mg v Placebo
Number of subjects included in analysis	350
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Least Squares (LS) Mean
Point estimate	-36.31

Confidence interval	
level	95 %
sides	2-sided
lower limit	-42.22
upper limit	-30.39
Variability estimate	Standard error of the mean
Dispersion value	3.019

Secondary: 2. Percent Change in Low Density Lipoprotein-Cholesterol (LDL-C) From Baseline to Day 180 [Martin/Hopkins]

End point title	2. Percent Change in Low Density Lipoprotein-Cholesterol (LDL-C) From Baseline to Day 180 [Martin/Hopkins]

End point description:

LS mean percent change from baseline to Day 180 in Low-Density Lipoprotein Cholesterol (LDL-C) in the obicetrapib group compared to the placebo group [Martin/Hopkins]. LDL-C value was calculated using the Martin/Hopkins equation unless TG >= 400 mg/dL or LDL-C <= 50 mg/dL; where, LDL-C value was measured directly by preparative ultracentrifugation (PUC).

End point type	Secondary

End point timeframe:

180 Days

End point values	Placebo	Obicetrapib 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	234		
Units: Percent Change from Baseline				
least squares mean (standard error)	5.98 (± 2.925)	-31.80 (± 2.054)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Obicetrapib 10 mg
Number of subjects included in analysis	352
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Least Squares (LS) Mean
Point estimate	-37.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-44.79
upper limit	-30.78

Variability estimate	Standard error of the mean
Dispersion value	3.572

Secondary: 3. Percent Change in Low Density Lipoprotein-Cholesterol (LDL-C) From Baseline to Day 365 [PUC]

End point title	3. Percent Change in Low Density Lipoprotein-Cholesterol (LDL-C) From Baseline to Day 365 [PUC]

End point description:

LS mean percent change from baseline to Day 365 in Low-Density Lipoprotein Cholesterol (LDL-C) in the obicetrapib group compared to the placebo group [PUC]. LDL-C level was measured by preparative ultracentrifugation (PUC).

End point type	Secondary

End point timeframe:

365 Days

End point values	Placebo	Obicetrapib 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	232		
Units: Percent Change from Baseline				
least squares mean (standard error)	10.30 (± 4.222)	-31.14 (± 2.544)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Obicetrapib 10 mg
Number of subjects included in analysis	350
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [1]
Method	ANCOVA
Parameter estimate	Least Squares (LS) Mean
Point estimate	-41.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-51.14
upper limit	-31.76
Variability estimate	Standard error of the mean
Dispersion value	4.938

Notes:

[1] - The hierarchical testing procedure would only be conducted if the previous secondary efficacy endpoint reached a statistically significant treatment effect at p-value<0.05

Secondary: 4. Percent Change in Apolipoprotein B (ApoB) From Baseline to Day 84

End point title	4. Percent Change in Apolipoprotein B (ApoB) From Baseline to Day 84

End point description:

LS mean percent change from baseline to Day 84 in apolipoprotein B (ApoB) in obicetrapib group compared to the placebo group.

End point type	Secondary

End point timeframe:

84 Days

End point values	Placebo	Obicetrapib 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	234		
Units: Percent Change from Baseline				
least squares mean (standard error)	2.93 (± 1.758)	-21.45 (± 1.219)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Obicetrapib 10 mg
Number of subjects included in analysis	352
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [2]
Method	ANCOVA
Parameter estimate	Least Squares (LS) Mean
Point estimate	-24.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.58
upper limit	-20.2
Variability estimate	Standard error of the mean
Dispersion value	2.136

Notes:

[2] - The hierarchical testing procedure would only be conducted if the previous secondary efficacy endpoint reached a statistically significant treatment effect at p-value<0.05

Secondary: 5. Percent Change in Apolipoprotein B (ApoB) From Baseline to Day 180

End point title	5. Percent Change in Apolipoprotein B (ApoB) From Baseline to Day 180

End point description:

LS mean percent change from baseline to Day 180 in apolipoprotein B (ApoB) in obicetrapib group compared to the placebo group

End point type	Secondary

End point timeframe:

180 Days

End point values	Placebo	Obicetrapib 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	234		
Units: Percent Change from Baseline				
least squares mean (standard error)	6.02 (± 2.127)	-18.30 (± 1.472)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Obicetrapib 10 mg
Number of subjects included in analysis	352
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [3]
Method	ANCOVA
Parameter estimate	Least Squares (LS) Mean
Point estimate	-24.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.38
upper limit	-19.25
Variability estimate	Standard error of the mean
Dispersion value	2.583

Notes:

[3] - The hierarchical testing procedure would only be conducted if the previous secondary efficacy endpoint reached a statistically significant treatment effect at p-value<0.05

Secondary: 6. Percent Change in Apolipoprotein B (ApoB) From Baseline to Day 365

End point title	6. Percent Change in Apolipoprotein B (ApoB) From Baseline to Day 365

End point description:

LS mean percent change from baseline to Day 365 in apolipoprotein B (ApoB) in obicetrapib group compared to the placebo group

End point type	Secondary

End point timeframe:

365 Days

End point values	Placebo	Obicetrapib 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	234		
Units: Percent Change from Baseline				
least squares mean (standard error)	8.15 (± 2.633)	-17.62 (± 1.663)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Obicetrapib 10 mg
Number of subjects included in analysis	352
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [4]
Method	ANCOVA
Parameter estimate	Least Squares (LS) Mean
Point estimate	-25.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.88
upper limit	-19.67
Variability estimate	Standard error of the mean
Dispersion value	3.114

Notes:

[4] - The hierarchical testing procedure would only be conducted if the previous secondary efficacy endpoint reached a statistically significant treatment effect at p-value<0.05

Secondary: 7. Percent Change in Non-HDL-C From Baseline to Day 84

End point title	7. Percent Change in Non-HDL-C From Baseline to Day 84

End point description:

LS mean percent change from baseline to Day 84 in Non-high-density Lipoprotein Cholesterol (Non-HDL-C) in obicetrapib group compared to the placebo group

End point type	Secondary

End point timeframe:

84 Days

End point values	Placebo	Obicetrapib 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	234		
Units: Percent Change from Baseline				
least squares mean (standard error)	2.83 (± 2.188)	-31.62 (± 1.520)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Obicetrapib 10 mg v Placebo
Number of subjects included in analysis	352
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [5]
Method	ANCOVA
Parameter estimate	Least Squares (LS) Mean
Point estimate	-34.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-39.67
upper limit	-29.24
Variability estimate	Standard error of the mean
Dispersion value	2.661

Notes:

[5] - The hierarchical testing procedure would only be conducted if the previous secondary efficacy endpoint reached a statistically significant treatment effect at p-value<0.05

Secondary: 8. Percent Change in Non-HDL-C From Baseline to Day 180

End point title	8. Percent Change in Non-HDL-C From Baseline to Day 180

End point description:

LS mean percent change from baseline to Day 180 in Non-high-density Lipoprotein Cholesterol (non-HDL-C) in obicetrapib group compared to the placebo group

End point type	Secondary

End point timeframe:

180 Days

End point values	Placebo	Obicetrapib 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	234		
Units: Percent Change from Baseline				
least squares mean (standard error)	5.92 (± 2.658)	-27.08 (± 1.855)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Obicetrapib 10 mg v Placebo
Number of subjects included in analysis	352
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [6]
Method	ANCOVA
Parameter estimate	Least Squares (LS) Mean
Point estimate	-33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-39.36
upper limit	-26.65
Variability estimate	Standard error of the mean
Dispersion value	3.241

Notes:

[6] - The hierarchical testing procedure would only be conducted if the previous secondary efficacy endpoint reached a statistically significant treatment effect at p-value<0.05

Secondary: 9. Percent Change in Non-HDL-C From Baseline to Day 365

End point title	9. Percent Change in Non-HDL-C From Baseline to Day 365

End point description:

LS mean percent change from baseline to Day 365 in Non-high-density Lipoprotein Cholesterol (non-HDL-C) in obicetrapib group compared to the placebo group

End point type	Secondary

End point timeframe:

365 Days

End point values	Placebo	Obicetrapib 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	234		
Units: Percent Change from Baseline				
least squares mean (standard error)	11.64 (± 3.905)	-25.84 (± 2.305)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Obicetrapib 10 mg

Number of subjects included in analysis	352
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [7]
Method	ANCOVA
Parameter estimate	Least Squares (LS) Mean
Point estimate	-37.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-46.38
upper limit	-28.58
Variability estimate	Standard error of the mean
Dispersion value	4.535

Notes:

[7] - The hierarchical testing procedure would only be conducted if the previous secondary efficacy endpoint reached a statistically significant treatment effect at p-value <0.05

Secondary: 10. Percent Change in HDL-C From Baseline to Day 84

End point title	10. Percent Change in HDL-C From Baseline to Day 84

End point description:

LS mean percent change from baseline to Day 84 in High-density Lipoprotein Cholesterol (HDL-C) in obicetrapib group compared to the placebo group

End point type	Secondary

End point timeframe:

84 Days

End point values	Placebo	Obicetrapib 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	234		
Units: Percent Change from Baseline				
least squares mean (standard error)	1.26 (± 5.078)	139.92 (± 3.614)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Obicetrapib 10 mg v Placebo
Number of subjects included in analysis	352
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [8]
Method	ANCOVA
Parameter estimate	Least Squares (LS) Mean
Point estimate	138.66

Confidence interval	
level	95 %
sides	2-sided
lower limit	126.42
upper limit	150.9
Variability estimate	Standard error of the mean
Dispersion value	6.244

Notes:

[8] - The hierarchical testing procedure would only be conducted if the previous secondary efficacy endpoint reached a statistically significant treatment effect at p-value <0.05

Secondary: 11. Percent Change in HDL-C From Baseline to Day 180

End point title	11. Percent Change in HDL-C From Baseline to Day 180

End point description:

LS mean percent change from baseline to Day 180 in High-density Lipoprotein Cholesterol (HDL-C) in obicetrapib group compared to the placebo group

End point type	Secondary

End point timeframe:

180 Days

End point values	Placebo	Obicetrapib 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	234		
Units: Percent Change from Baseline				
least squares mean (standard error)	2.63 (± 5.484)	133.83 (± 3.730)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Obicetrapib 10 mg
Number of subjects included in analysis	352
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [9]
Method	ANCOVA
Parameter estimate	Least Squares (LS) Mean
Point estimate	131.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	118.27
upper limit	144.13
Variability estimate	Standard error of the mean
Dispersion value	6.595

Notes:

[9] - The hierarchical testing procedure would only be conducted if the previous secondary efficacy endpoint reached a statistically significant treatment effect at p-value <0.05

Secondary: 12. Percent Change in HDL-C From Baseline to Day 365

End point title	12. Percent Change in HDL-C From Baseline to Day 365

End point description:

LS mean percent change from baseline to Day 365 in High-density Lipoprotein Cholesterol (HDL-C) in obicetrapib group compared to the placebo group

End point type	Secondary

End point timeframe:

365 Days

End point values	Placebo	Obicetrapib 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	234		
Units: Percent Change from Baseline				
least squares mean (standard error)	6.28 (± 5.994)	127.67 (± 4.222)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Obicetrapib 10 mg
Number of subjects included in analysis	352
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [10]
Method	ANCOVA
Parameter estimate	Least Squares (LS) Mean
Point estimate	121.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	107.02
upper limit	135.76
Variability estimate	Standard error of the mean
Dispersion value	7.333

Notes:

[10] - The hierarchical testing procedure would only be conducted if the previous secondary efficacy endpoint reached a statistically significant treatment effect at p-value <0.05

Secondary: 13. Percent Change in Lp(a) From Baseline to Day 84

End point title	13. Percent Change in Lp(a) From Baseline to Day 84

End point description:

LS mean percent change from baseline to Day 84 in Lipoprotein (a) [Lp(a)] in obicetrapib group compared to the placebo group

End point type	Secondary

End point timeframe:

84 Days

End point values	Placebo	Obicetrapib 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	234		
Units: Percent Change from Baseline				
least squares mean (standard error)	10.52 (± 9.413)	-35.42 (± 4.527)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Obicetrapib 10 mg
Number of subjects included in analysis	352
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [11]
Method	ANCOVA
Parameter estimate	Least Squares (LS) Mean
Point estimate	-45.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	-65.88
upper limit	-26
Variability estimate	Standard error of the mean
Dispersion value	10.14

Notes:

[11] - The hierarchical testing procedure would only be conducted if the previous secondary efficacy endpoint reached a statistically significant treatment effect at p-value<0.05

Secondary: 14. Percent Change in Lp(a) From Baseline to Day 365

End point title	14. Percent Change in Lp(a) From Baseline to Day 365

End point description:

LS mean percent change from baseline to Day 365 in Lipoprotein (a) [Lp(a)] in obicetrapib group compared to the placebo group

End point type	Secondary

End point timeframe:

365 Days

End point values	Placebo	Obicetrapib 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	234		
Units: Percent Change from Baseline				
least squares mean (standard error)	24.37 (± 37.111)	-29.93 (± 11.224)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Obicetrapib 10 mg
Number of subjects included in analysis	352
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1648 [12]
Method	ANCOVA
Parameter estimate	Least Squares (LS) Mean
Point estimate	-54.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-131.13
upper limit	22.53
Variability estimate	Standard error of the mean
Dispersion value	38.924

Notes:

[12] - The hierarchical testing procedure would only be conducted if the previous secondary efficacy endpoint reached a statistically significant treatment effect at p-value<0.05; therefore hierarchical testing was stopped for subsequent secondary endpoints

Secondary: 15. Percent Change in Total Cholesterol From Baseline to Day 84

End point title	15. Percent Change in Total Cholesterol From Baseline to Day 84

End point description:

LS mean percent change from baseline to Day 84 in Total Cholesterol (TC) in obicetrapib group compared to the placebo group

End point type	Secondary

End point timeframe:

84 Days

End point values	Placebo	Obicetrapib 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	234		
Units: Percent Change from Baseline				
least squares mean (standard error)	2.34 (± 1.796)	12.09 (± 1.268)		

Statistical analyses

No statistical analyses for this end point

Secondary: 16. Percent Change in Total Cholesterol From Baseline to Day 180

End point title	16. Percent Change in Total Cholesterol From Baseline to Day 180

End point description:

LS mean percent change from baseline to Day 180 in Total Cholesterol in obicetrapib group compared to the placebo group

End point type	Secondary

End point timeframe:

180 Days

End point values	Placebo	Obicetrapib 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	234		
Units: Percent Change from Baseline				
least squares mean (standard error)	4.44 (± 2.043)	14.43 (± 1.438)		

Statistical analyses

No statistical analyses for this end point

Secondary: 17. Percent Change in Total Cholesterol From Baseline to Day 365

End point title	17. Percent Change in Total Cholesterol From Baseline to Day 365

End point description:

LS mean percent change from baseline to Day 365 in Total Cholesterol in obicetrapib group compared to the placebo group

End point type	Secondary

End point timeframe:

365 Days

End point values	Placebo	Obicetrapib 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	234		
Units: Percent Change from Baseline				
least squares mean (standard error)	9.32 (± 2.801)	13.92 (± 1.684)		

Statistical analyses

No statistical analyses for this end point

Secondary: 18. Percent Change in Triglycerides From Baseline to Day 84

End point title	18. Percent Change in Triglycerides From Baseline to Day 84

End point description:

LS mean percent change from baseline to Day 84 in Triglycerides in obicetrapib group compared to the placebo group

End point type	Secondary

End point timeframe:

84 Days

End point values	Placebo	Obicetrapib 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	234		
Units: Percent Change from Baseline				
least squares mean (standard error)	10.16 (± 4.207)	-1.57 (± 2.580)		

Statistical analyses

No statistical analyses for this end point

Secondary: 19. Percent Change in Triglycerides From Baseline to Day 180

End point title	19. Percent Change in Triglycerides From Baseline to Day 180

End point description:

LS mean percent change from baseline to Day 180 in Triglycerides in obicetrapib group compared to the placebo group

End point type	Secondary

End point timeframe:

180 Days

End point values	Placebo	Obicetrapib 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	234		
Units: Percent Change from Baseline				
least squares mean (standard error)	12.43 (± 4.178)	4.49 (± 2.885)		

Statistical analyses

No statistical analyses for this end point

Secondary: 20. Percent Change in Triglycerides From Baseline to Day 365

End point title	20. Percent Change in Triglycerides From Baseline to Day 365

End point description:

LS mean percent change from baseline to Day 365 in Triglycerides in obicetrapib group compared to the placebo group

End point type	Secondary

End point timeframe:

365 Days

End point values	Placebo	Obicetrapib 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	234		
Units: Percent Change from Baseline				
least squares mean (standard error)	7.39 (± 5.642)	2.27 (± 3.219)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose of study drug up to Week 54	
Adverse event reporting additional description:	
Safety Population included all participants who received at least 1 dose of any study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
one placebo tablet once daily; Placebo: placebo tablet made to resemble active	
Reporting group title	Obicetrapib 10 mg
Reporting group description:	
one 10 mg Obicetrapib tablet once daily; Obicetrapib: 10 mg Obicetrapib tablet	

Serious adverse events	Placebo	Obicetrapib 10 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 118 (6.78%)	13 / 234 (5.56%)	
number of deaths (all causes)	2	3	
number of deaths resulting from adverse events	2	3	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 118 (0.00%)	1 / 234 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salivary gland adenoma			
subjects affected / exposed	0 / 118 (0.00%)	1 / 234 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Accident			

subjects affected / exposed	0 / 118 (0.00%)	1 / 234 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Rib fracture			
subjects affected / exposed	1 / 118 (0.85%)	0 / 234 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Angiopathy			
subjects affected / exposed	0 / 118 (0.00%)	1 / 234 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Deep vein thrombosis			
subjects affected / exposed	1 / 118 (0.85%)	0 / 234 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 118 (0.85%)	1 / 234 (0.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	2 / 118 (1.69%)	0 / 234 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	0 / 118 (0.00%)	2 / 234 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 118 (0.00%)	1 / 234 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden cardiac death			

subjects affected / exposed	1 / 118 (0.85%)	0 / 234 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 118 (0.00%)	1 / 234 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 118 (0.00%)	1 / 234 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death	Additional description: From natural causes		
subjects affected / exposed	1 / 118 (0.85%)	0 / 234 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	0 / 118 (0.00%)	1 / 234 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	1 / 118 (0.85%)	0 / 234 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal fistula			
subjects affected / exposed	1 / 118 (0.85%)	0 / 234 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			

subjects affected / exposed	1 / 118 (0.85%)	0 / 234 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 118 (0.00%)	1 / 234 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 118 (0.00%)	2 / 234 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumothorax			
subjects affected / exposed	1 / 118 (0.85%)	0 / 234 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 118 (0.00%)	1 / 234 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal stenosis			
subjects affected / exposed	0 / 118 (0.00%)	1 / 234 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Diabetic gangrene			
subjects affected / exposed	1 / 118 (0.85%)	0 / 234 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			

subjects affected / exposed	0 / 118 (0.00%)	1 / 234 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 118 (0.00%)	1 / 234 (0.43%)	
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: 2 %

Non-serious adverse events	Placebo	Obicetrapib 10 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	52 / 118 (44.07%)	95 / 234 (40.60%)	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	5 / 118 (4.24%)	3 / 234 (1.28%)	
occurrences (all)	6	4	
Vascular disorders			
Hypertension			
subjects affected / exposed	8 / 118 (6.78%)	14 / 234 (5.98%)	
occurrences (all)	10	14	
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 118 (5.08%)	7 / 234 (2.99%)	
occurrences (all)	8	9	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	7 / 118 (5.93%)	2 / 234 (0.85%)	
occurrences (all)	7	2	
Gastrointestinal disorders			
Diarrhea			
subjects affected / exposed	8 / 118 (6.78%)	9 / 234 (3.85%)	
occurrences (all)	9	10	
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	3 / 118 (2.54%)	5 / 234 (2.14%)	
occurrences (all)	3	5	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 118 (2.54%)	9 / 234 (3.85%)	
occurrences (all)	4	9	
Back pain			
subjects affected / exposed	6 / 118 (5.08%)	7 / 234 (2.99%)	
occurrences (all)	6	7	
Myalgia			
subjects affected / exposed	1 / 118 (0.85%)	10 / 234 (4.27%)	
occurrences (all)	1	10	
Pain in extremity			
subjects affected / exposed	4 / 118 (3.39%)	6 / 234 (2.56%)	
occurrences (all)	4	8	
Infections and infestations			
COVID-19			
subjects affected / exposed	8 / 118 (6.78%)	15 / 234 (6.41%)	
occurrences (all)	8	16	
Influenza			
subjects affected / exposed	7 / 118 (5.93%)	21 / 234 (8.97%)	
occurrences (all)	7	22	
Nasopharyngitis			
subjects affected / exposed	5 / 118 (4.24%)	15 / 234 (6.41%)	
occurrences (all)	5	17	
Upper respiratory tract infection			
subjects affected / exposed	4 / 118 (3.39%)	12 / 234 (5.13%)	
occurrences (all)	4	15	
Urinary tract infection			
subjects affected / exposed	5 / 118 (4.24%)	7 / 234 (2.99%)	
occurrences (all)	5	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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/38705341