Clinical trial results:
A Phase 2b, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of MK-0616 in Adults With Hypercholesterolemia

Summary

EudraCT number	2021-005221-24
Trial protocol	DE NO
Global end of trial date	28 November 2022

Results information

Result version number	v1 (current)
This version publication date	01 December 2023
First version publication date	01 December 2023

Trial information

Trial identification

Sponsor protocol code	0616-008

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05261126
WHO universal trial number (UTN)	-
Other trial identifiers	jRCT2031210701: jRCT

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme LLC
Sponsor organisation address	126 East Lincoln Avenue, P.O. Box 2000, Rahway, NJ, United States, 07065
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 November 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 November 2022
Global end of trial reached?	Yes
Global end of trial date	28 November 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the efficacy and safety of MK-0616, an oral PCSK9 inhibitor, in lowering low-density lipoprotein cholesterol (LDL-C) in participants with hypercholesterolemia. The primary hypothesis is that at least one of the four doses of MK-0616 tested in this study is superior to placebo on percent change from baseline in LDL-C at Week 8.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 March 2022
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	Germany: 19
Country: Number of subjects enrolled	Japan: 42
Country: Number of subjects enrolled	Mexico: 119
Country: Number of subjects enrolled	Norway: 21
Country: Number of subjects enrolled	Korea, Republic of: 19
Country: Number of subjects enrolled	Turkey: 9
Country: Number of subjects enrolled	United Kingdom: 14
Country: Number of subjects enrolled	United States: 138
Worldwide total number of subjects	381
EEA total number of subjects	40

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)	223
From 65 to 84 years	158
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Of 668 participants screened for inclusion, 381 were randomized 1:1:1:1:1 to receive MK-0616 6 mg, 12 mg, 18 mg, 30 mg, or placebo. Of the 381 randomized participants, one participant did not receive at least one dose of study intervention.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	MK-0616 6 mg

Arm description:

Participants received 6 mg of MK-0616 orally once daily (QD) for 8 weeks

Arm type	Experimental
Investigational medicinal product name	MK-0616
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

6 mg MK-0616 was administered orally in capsule form for up to 8 weeks.

Arm title	MK-0616 12 mg

Arm description:

Participants received 12 mg of MK-0616 orally QD for 8 weeks

Arm type	Experimental
Investigational medicinal product name	MK-0616
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

12 mg MK-0616 was administered orally in capsule form for up to 8 weeks.

Arm title	MK-0616 18 mg

Arm description:

Participants received 18 mg of MK-0616 orally QD for 8 weeks

Arm type	Experimental
Investigational medicinal product name	MK-0616
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
18 mg MK-0616 was administered orally in capsule form for up to 8 weeks.

Arm title	MK-0616 30 mg
Arm description:	
Participants received 30 mg of MK-0616 orally QD for 8 weeks	
Arm type	Experimental
Investigational medicinal product name	MK-0616
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
30 mg MK-0616 was administered orally in capsule form for up to 8 weeks.	
Arm title	Placebo
Arm description:	
Participants received MK-0616-matching placebo orally QD for 8 weeks	
Arm type	Placebo
Investigational medicinal product name	Placebo to MK-0616
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
MK-0616 matching placebo was administered orally in capsule form for up to 8 weeks.	

Number of subjects in period 1	MK-0616 6 mg	MK-0616 12 mg	MK-0616 18 mg
Started	77	76	76
Treated	77	76	76
Completed	75	76	74
Not completed	2	0	2
Physician decision	1	-	-
Consent withdrawn by subject	1	-	1
Screen Failure	-	-	-
Death	-	-	1
Not Recorded	-	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	MK-0616 30 mg	Placebo
Started	76	76
Treated	76	75

Completed	74	74
Not completed	2	2
Physician decision	-	-
Consent withdrawn by subject	1	-
Screen Failure	-	1
Death	-	-
Not Recorded	1	-
Lost to follow-up	-	1

Baseline characteristics

Reporting groups	
Reporting group title	MK-0616 6 mg
Reporting group description:	
Participants received 6 mg of MK-0616 orally once daily (QD) for 8 weeks	
Reporting group title	MK-0616 12 mg
Reporting group description:	
Participants received 12 mg of MK-0616 orally QD for 8 weeks	
Reporting group title	MK-0616 18 mg
Reporting group description:	
Participants received 18 mg of MK-0616 orally QD for 8 weeks	
Reporting group title	MK-0616 30 mg
Reporting group description:	
Participants received 30 mg of MK-0616 orally QD for 8 weeks	
Reporting group title	Placebo
Reporting group description:	
Participants received MK-0616-matching placebo orally QD for 8 weeks	

Reporting group values	MK-0616 6 mg	MK-0616 12 mg	MK-0616 18 mg
Number of subjects	77	76	76
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)	39	47	42
From 65-84 years	38	29	34
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	61.7	62.0	62.0
standard deviation	± 10.3	± 9.4	± 9.2
Sex: Female, Male Units: Participants			
Female	38	35	39
Male	39	41	37
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	4	5	5
Asian	18	13	11
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	4	5	2
White	49	48	55

More than one race	2	5	3
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	26	29	31
Not Hispanic or Latino	51	46	45
Unknown or Not Reported	0	1	0
Randomization Strata: Background Statin Dose			
Participants were stratified by the following background statin dose: no statin therapy, low-intensity to moderate-intensity statin therapy, or high-intensity statin therapy.			
Units: Subjects			
No Statin Therapy	30	29	31
Low- to Moderate-intensity Statin Therapy	27	27	26
High-intensity Statin Therapy	20	20	19
Randomization Strata: Renal Function			
Estimated glomerular filtration rate (eGFR) was calculated using Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) Creatinine. Participants were stratified by the following renal function at baseline: eGFR ≥60 vs <60 ml/min/1.73 m^2.			
Units: Subjects			
eGFR ≥60 ml/min/1.73 m^2	71	72	72
eGFR <60 ml/min/1.73 m^2	6	4	4
Baseline Low-density Lipoprotein Cholesterol (LDL-C)			
Blood samples were taken at baseline to determine baseline LDL-C levels.			
Units: mg/dL			
arithmetic mean	116.5	117.3	123.7
standard deviation	± 37.0	± 36.4	± 35.1

Reporting group values	MK-0616 30 mg	Placebo	Total
Number of subjects	76	76	381
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)	44	51	223
From 65-84 years	32	25	158
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	60.9	60.6	
standard deviation	± 10.2	± 9.3	-
Sex: Female, Male			
Units: Participants			
Female	38	38	188
Male	38	38	193

Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	2	5	21
Asian	13	8	63
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	9	4	24
White	44	54	250
More than one race	8	5	23
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	31	37	154
Not Hispanic or Latino	45	38	225
Unknown or Not Reported	0	1	2
Randomization Strata: Background Statin Dose			
Participants were stratified by the following background statin dose: no statin therapy, low-intensity to moderate-intensity statin therapy, or high-intensity statin therapy.			
Units: Subjects			
No Statin Therapy	30	30	150
Low- to Moderate-intensity Statin Therapy	26	26	132
High-intensity Statin Therapy	20	20	99
Randomization Strata: Renal Function			
Estimated glomerular filtration rate (eGFR) was calculated using Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) Creatinine. Participants were stratified by the following renal function at baseline: eGFR ≥60 vs <60 ml/min/1.73 m^2.			
Units: Subjects			
eGFR ≥60 ml/min/1.73 m^2	71	71	357
eGFR <60 ml/min/1.73 m^2	5	5	24
Baseline Low-density Lipoprotein Cholesterol (LDL-C)			
Blood samples were taken at baseline to determine baseline LDL-C levels.			
Units: mg/dL			
arithmetic mean	119.4	120.7	
standard deviation	± 36.7	± 28.3	-

End points

End points reporting groups	
Reporting group title	MK-0616 6 mg
Reporting group description:	
Participants received 6 mg of MK-0616 orally once daily (QD) for 8 weeks	
Reporting group title	MK-0616 12 mg
Reporting group description:	
Participants received 12 mg of MK-0616 orally QD for 8 weeks	
Reporting group title	MK-0616 18 mg
Reporting group description:	
Participants received 18 mg of MK-0616 orally QD for 8 weeks	
Reporting group title	MK-0616 30 mg
Reporting group description:	
Participants received 30 mg of MK-0616 orally QD for 8 weeks	
Reporting group title	Placebo
Reporting group description:	
Participants received MK-0616-matching placebo orally QD for 8 weeks	

Primary: Percent Change from Baseline in Low-density Lipoprotein Cholesterol (LDL-C) at Week 8	
End point title	Percent Change from Baseline in Low-density Lipoprotein Cholesterol (LDL-C) at Week 8
End point description:	
Blood samples were collected at baseline and after 8 weeks of treatment to assess mean percent change in LDL-C. Based on a constrained longitudinal analysis (cLDA) model including terms for treatment, time, baseline statin intensity, baseline renal function, and the interaction of treatment by time. The percent change from baseline in LDL-C at week 8 was reported. All randomized participants who received at least one dose of study intervention, had at least one observation for the analysis endpoint, and had baseline data were analyzed.	
End point type	Primary
End point timeframe:	
Baseline and up to Week 8	

End point values	MK-0616 6 mg	MK-0616 12 mg	MK-0616 18 mg	MK-0616 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	75	75	74	73
Units: Percentage Change				
least squares mean (confidence interval 95%)	-40.0 (-45.2 to -34.8)	-54.5 (-59.8 to -49.2)	-57.9 (-63.2 to -52.6)	-59.7 (-65.0 to -54.5)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	72			

Units: Percentage Change				
least squares mean (confidence interval 95%)	1.2 (-4.1 to 6.5)			

Statistical analyses

Statistical analysis title	Percent Change from Baseline in LDL-C

Statistical analysis description:

One-sided p-value and difference in least squares means based on a cLDA model including terms for treatment, time, baseline statin intensity, baseline renal function, and the interaction of treatment by time.

Comparison groups	MK-0616 6 mg v Placebo
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	cLDA
Parameter estimate	Difference in Least Squares Means
Point estimate	-41.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-47.8
upper limit	-34.7

Statistical analysis title	Percent Change from Baseline in LDL-C

Statistical analysis description:

One-sided p-value and difference in least squares means based on a cLDA model including terms for treatment, time, baseline statin intensity, baseline renal function, and the interaction of treatment by time.

Comparison groups	MK-0616 12 mg v Placebo
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	cLDA
Parameter estimate	Difference in Least Squares Means
Point estimate	-55.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-62.3
upper limit	-49.1

Statistical analysis title	Percent Change from Baseline in LDL-C

Statistical analysis description:

One-sided p-value and difference in least squares means based on a cLDA model including terms for treatment, time, baseline statin intensity, baseline renal function, and the interaction of treatment by time.

Comparison groups	MK-0616 18 mg v Placebo
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	cLDA
Parameter estimate	Difference in Least Squares Means
Point estimate	-59.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-65.7
upper limit	-52.5

Statistical analysis title	Percent Change from Baseline in LDL-C

Statistical analysis description:

One-sided p-value and difference in least squares means based on a cLDA model including terms for treatment, time, baseline statin intensity, baseline renal function, and the interaction of treatment by time.

Comparison groups	MK-0616 30 mg v Placebo
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	cLDA
Parameter estimate	Difference in Least Squares Means
Point estimate	-60.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-67.6
upper limit	-54.3

Primary: Percentage of Participants Who Experienced One or More Adverse Events (AEs)

End point title	Percentage of Participants Who Experienced One or More Adverse Events (AEs)

End point description:

An AE was any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. An AE could therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a study intervention. The percentage of participants who experienced at least one AE was reported. All randomized participants who received at least one dose of study intervention were analyzed.

End point type	Primary

End point timeframe:
Up to approximately 17 Weeks

End point values	MK-0616 6 mg	MK-0616 12 mg	MK-0616 18 mg	MK-0616 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	77	76	76	76
Units: Percentage of Participants				
number (not applicable)	44.2	39.5	43.4	42.1

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	75			
Units: Percentage of Participants				
number (not applicable)	44.0			

Statistical analyses

Statistical analysis title	Difference in Percentage of Participants with AEs
Statistical analysis description: Difference in percentage (MK-0616 6 mg minus Placebo) based on Miettinen & Nurminen method.	
Comparison groups	MK-0616 6 mg v Placebo
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percentage
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.5
upper limit	15.8

Statistical analysis title	Difference in Percentage of Participants with AEs
Statistical analysis description: Difference in percentage (MK-0616 12 mg minus Placebo) based on Miettinen & Nurminen method.	
Comparison groups	MK-0616 12 mg v Placebo

Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percentage
Point estimate	-4.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20
upper limit	11.2

Statistical analysis title	Difference in Percentage of Participants with AEs
Statistical analysis description: Difference in percentage (MK-0616 18 mg minus Placebo) based on Miettinen & Nurminen method.	
Comparison groups	MK-0616 18 mg v Placebo
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percentage
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.3
upper limit	15.1

Statistical analysis title	Difference in Percentage of Participants with AEs
Statistical analysis description: Difference in percentage (MK-0616 30 mg minus Placebo) based on Miettinen & Nurminen method.	
Comparison groups	MK-0616 30 mg v Placebo
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percentage
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.5
upper limit	13.8

Primary: Percentage of Participants Who Discontinued Study Intervention Due to AEs

End point title	Percentage of Participants Who Discontinued Study

	Intervention Due to AEs[1]

End point description:

An AE was any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. An AE could therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a study intervention. The percentage of participants who discontinued study intervention due to AEs was reported. All randomized participants who received at least one dose of study intervention were analyzed.

End point type	Primary

End point timeframe:

Up to approximately 9 Weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was performed due to a small sample size.

End point values	MK-0616 6 mg	MK-0616 12 mg	MK-0616 18 mg	MK-0616 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	77	76	76	76
Units: Percentage of Participants				
number (not applicable)	2.6	0.0	2.6	2.6

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	75			
Units: Percentage of Participants				
number (not applicable)	1.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in Apolipoprotein B (ApoB) at Week 8

End point title	Percent Change from Baseline in Apolipoprotein B (ApoB) at Week 8

End point description:

Blood samples were collected at baseline and after 8 weeks of treatment to assess mean percent change in ApoB. The least square mean and 95% CI were obtained from fitting a cLDA model including terms for treatment, time, baseline statin intensity, baseline renal function, and the interaction of treatment by time. The percent change from baseline in ApoB at week 8 was reported. All randomized participants who received at least one dose of study intervention, had at least one observation for the analysis endpoint, and had baseline data were analyzed.

End point type	Secondary

End point timeframe:

Baseline and up to Week 8

End point values	MK-0616 6 mg	MK-0616 12 mg	MK-0616 18 mg	MK-0616 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	76	75	74	74
Units: Percentage Change				
least squares mean (confidence interval 95%)	-32.8 (-37.6 to -27.9)	-45.8 (-50.7 to -40.9)	-48.7 (-53.6 to -43.8)	-51.8 (-56.7 to -47.0)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	72			
Units: Percentage Change				
least squares mean (confidence interval 95%)	0.0 (-4.9 to 4.9)			

Statistical analyses

Statistical analysis title	Percent Change from Baseline in ApoB

Statistical analysis description:

One-sided p-value and difference in least squares means based on a cLDA model including terms for treatment, time, baseline statin intensity, baseline renal function, and the interaction of treatment by time.

Comparison groups	MK-0616 6 mg v Placebo
Number of subjects included in analysis	148
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	cLDA
Parameter estimate	Difference in Least Squares Means
Point estimate	-32.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-38.6
upper limit	-26.9

Statistical analysis title	Percent Change from Baseline in ApoB

Statistical analysis description:

One-sided p-value and difference in least squares means based on a cLDA model including terms for treatment, time, baseline statin intensity, baseline renal function, and the interaction of treatment by time.

Comparison groups	MK-0616 12 mg v Placebo

Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	cLDA
Parameter estimate	Difference in Least Squares Means
Point estimate	-45.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-51.7
upper limit	-39.9

Statistical analysis title	Percent Change from Baseline in ApoB

Statistical analysis description:

One-sided p-value and difference in least squares means based on a cLDA model including terms for treatment, time, baseline statin intensity, baseline renal function, and the interaction of treatment by time.

Comparison groups	MK-0616 18 mg v Placebo
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	cLDA
Parameter estimate	Difference in Least Squares Means
Point estimate	-48.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-54.6
upper limit	-42.8

Statistical analysis title	Percent Change from Baseline in ApoB

Statistical analysis description:

One-sided p-value and difference in least squares means based on a cLDA model including terms for treatment, time, baseline statin intensity, baseline renal function, and the interaction of treatment by time.

Comparison groups	MK-0616 30 mg v Placebo
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	cLDA
Parameter estimate	Difference in Least Square Means
Point estimate	-51.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-57.7
upper limit	-45.9

Secondary: Percent Change from Baseline in Non-High-density Lipoprotein Cholesterol (non-HDL-C) at Week 8

End point title	Percent Change from Baseline in Non-High-density Lipoprotein Cholesterol (non-HDL-C) at Week 8

End point description:

Blood samples were collected at baseline and after 8 weeks of treatment to assess mean percent change in non-HDL-C. The least square mean and 95% CI were obtained from fitting a cLDA model including terms for treatment, time, baseline statin intensity, baseline renal function, and the interaction of treatment by time. The percent change from baseline in non-HDL-C at week 8 was reported. All randomized participants who received at least one dose of study intervention, had at least one observation for the analysis endpoint, and had baseline data were analyzed.

End point type	Secondary

End point timeframe:

Baseline and up to Week 8

End point values	MK-0616 6 mg	MK-0616 12 mg	MK-0616 18 mg	MK-0616 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	74	76	74	73
Units: Percentage Change				
least squares mean (confidence interval 95%)	-34.4 (-39.6 to -29.2)	-49.0 (-54.3 to -43.7)	-51.8 (-57.1 to -46.4)	-54.3 (-59.6 to -49.1)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	72			
Units: Percentage Change				
least squares mean (confidence interval 95%)	1.5 (-3.9 to 6.8)			

Statistical analyses

Statistical analysis title	Percent Change from Baseline in Non-HDL-C

Statistical analysis description:

One-sided p-value and difference in least squares means based on a cLDA model including terms for treatment, time, baseline statin intensity, baseline renal function, and the interaction of treatment by time.

Comparison groups	MK-0616 6 mg v Placebo

Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	cLDA
Parameter estimate	Difference in Least Squares Means
Point estimate	-35.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-42.4
upper limit	-29.4

Statistical analysis title	Percent Change from Baseline in Non-HDL-C

Statistical analysis description:

One-sided p-value and difference in least squares means based on a cLDA model including terms for treatment, time, baseline statin intensity, baseline renal function, and the interaction of treatment by time.

Comparison groups	MK-0616 12 mg v Placebo
Number of subjects included in analysis	148
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	cLDA
Parameter estimate	Difference in Least Squares Means
Point estimate	-50.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-57
upper limit	-44

Statistical analysis title	Percent Change from Baseline in Non-HDL-C

Statistical analysis description:

One-sided p-value and difference in least squares means based on a cLDA model including terms for treatment, time, baseline statin intensity, baseline renal function, and the interaction of treatment by time.

Comparison groups	MK-0616 18 mg v Placebo
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	cLDA
Parameter estimate	Difference in Least Squares Means
Point estimate	-53.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-59.7
upper limit	-46.7

Statistical analysis title	Percent Change from Baseline in Non-HDL-C

Statistical analysis description:

One-sided p-value and difference in least squares means based on a cLDA model including terms for treatment, time, baseline statin intensity, baseline renal function, and the interaction of treatment by time.

Comparison groups	MK-0616 30 mg v Placebo
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	cLDA
Parameter estimate	Difference in Least Squares Means
Point estimate	-55.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-62.3
upper limit	-49.3

Secondary: Percentage of Participants with LDL-C Value at Goal at Week 8

End point title	Percentage of Participants with LDL-C Value at Goal at Week 8

End point description:

LDL-C goal was defined as: LDL-C <70 mg/dL (<1.81 mmol/L) in participants with clinical atherosclerotic cardiovascular disease (ASCVD), LDL-C <100 mg/dL (<2.59 mmol/L) in participants with an ASCVD risk-equivalent and/or a 10-year risk of having an ASCVD event that is ≥7.5%, OR LDL-C <130 mg/dL (<3.37mmol/L) in participants with a 10-year risk of having an ASCVD event that is ≥5.0% and <7.5%. The percentage of participants with LDL-C value at goal at week 8 were reported. All randomized participants who received at least one dose of study intervention and had at least one observation for the analysis endpoint were analyzed.

End point type	Secondary

End point timeframe:

Week 8

End point values	MK-0616 6 mg	MK-0616 12 mg	MK-0616 18 mg	MK-0616 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	77	76	76	76
Units: Percentage of Participants				
number (not applicable)	80.5	85.5	90.8	90.8

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	75			
Units: Percentage of Participants				
number (not applicable)	9.3			

Statistical analyses

Statistical analysis title	Participants with LDL-C Value at Goal
Statistical analysis description:	
One-sided p-value and difference in percentage (MK-0616 6 mg minus Placebo) based on Miettinen & Nurminen method, with sample size weighting, stratified by background statin intensity.	
Comparison groups	MK-0616 6 mg v Placebo
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	69.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	56.2
upper limit	79

Statistical analysis title	Participants with LDL-C Value at Goal
Statistical analysis description:	
One-sided p-value and difference in percentage (MK-0616 12 mg minus Placebo) based on Miettinen & Nurminen method, with sample size weighting, stratified by background statin intensity.	
Comparison groups	MK-0616 12 mg v Placebo
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Difference in Percentage
Point estimate	75.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	62.9
upper limit	84

Statistical analysis title	Participants with LDL-C Value at Goal
Statistical analysis description:	
One-sided p-value and difference in percentage (MK-0616 18 mg minus Placebo) based on Miettinen & Nurminen method, with sample size weighting, stratified by background statin intensity.	
Comparison groups	MK-0616 18 mg v Placebo
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Difference in Percentage
Point estimate	79.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	67.1
upper limit	87.1

Statistical analysis title	Participants with LDL-C Value at Goal
Statistical analysis description:	
One-sided p-value and difference in percentage (MK-0616 30 mg minus Placebo) based on Miettinen & Nurminen method, with sample size weighting, stratified by background statin intensity.	
Comparison groups	MK-0616 30 mg v Placebo
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Difference in Percentage
Point estimate	79.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	67.9
upper limit	87.4

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to approximately 17 weeks

Adverse event reporting additional description:

The population analyzed for the All-Cause Mortality was all randomized participants. The population analyzed for AEs was all randomized participants who received at least one dose of study treatment, corresponding to the study treatment they actually received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	MK-0616 12 mg

Reporting group description:

Participants received 12 mg of MK-0616 orally QD for 8 weeks

Reporting group title	MK-0616 6 mg

Reporting group description:

Participants received 6 mg of MK-0616 orally QD for 8 weeks

Reporting group title	MK-0616 30 mg

Reporting group description:

Participants received 30 mg of MK-0616 orally QD for 8 weeks

Reporting group title	Placebo

Reporting group description:

Participants received MK-0616-matching placebo orally QD for 8 weeks

Reporting group title	MK-0616 18 mg

Reporting group description:

Participants received 18 mg of MK-0616 orally QD for 8 weeks

Serious adverse events	MK-0616 12 mg	MK-0616 6 mg	MK-0616 30 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 76 (3.95%)	1 / 77 (1.30%)	2 / 76 (2.63%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Diffuse large B-cell lymphoma			
subjects affected / exposed	0 / 76 (0.00%)	0 / 77 (0.00%)	1 / 76 (1.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Road traffic accident			

subjects affected / exposed	0 / 76 (0.00%)	0 / 77 (0.00%)	0 / 76 (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
Multiple injuries			
subjects affected / exposed	0 / 76 (0.00%)	0 / 77 (0.00%)	1 / 76 (1.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 77 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute left ventricular failure			
subjects affected / exposed	0 / 76 (0.00%)	0 / 77 (0.00%)	0 / 76 (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
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 76 (0.00%)	1 / 77 (1.30%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 77 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory distress			
subjects affected / exposed	0 / 76 (0.00%)	0 / 77 (0.00%)	0 / 76 (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
Psychiatric disorders			
Post-traumatic stress disorder			

subjects affected / exposed	0 / 76 (0.00%)	0 / 77 (0.00%)	1 / 76 (1.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 76 (1.32%)	0 / 77 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo	MK-0616 18 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 75 (0.00%)	2 / 76 (2.63%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Diffuse large B-cell lymphoma			
subjects affected / exposed	0 / 75 (0.00%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	0 / 75 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Multiple injuries			
subjects affected / exposed	0 / 75 (0.00%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute left ventricular failure			

subjects affected / exposed	0 / 75 (0.00%)	1 / 76 (1.32%)	
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			
Non-cardiac chest pain			
subjects affected / exposed	0 / 75 (0.00%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory distress			
subjects affected / exposed	0 / 75 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Post-traumatic stress disorder			
subjects affected / exposed	0 / 75 (0.00%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 75 (0.00%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	MK-0616 12 mg	MK-0616 6 mg	MK-0616 30 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 76 (17.11%)	11 / 77 (14.29%)	8 / 76 (10.53%)
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 76 (3.95%)	0 / 77 (0.00%)	0 / 76 (0.00%)
occurrences (all)	3	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 76 (1.32%)	5 / 77 (6.49%)	1 / 76 (1.32%)
occurrences (all)	1	5	2
Dyspepsia			
subjects affected / exposed	5 / 76 (6.58%)	1 / 77 (1.30%)	0 / 76 (0.00%)
occurrences (all)	5	1	0
Nausea			
subjects affected / exposed	1 / 76 (1.32%)	1 / 77 (1.30%)	2 / 76 (2.63%)
occurrences (all)	1	1	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 76 (5.26%)	0 / 77 (0.00%)	2 / 76 (2.63%)
occurrences (all)	5	0	2
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 76 (1.32%)	6 / 77 (7.79%)	4 / 76 (5.26%)
occurrences (all)	1	6	4

Non-serious adverse events	Placebo	MK-0616 18 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 75 (20.00%)	15 / 76 (19.74%)	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	5 / 75 (6.67%)	1 / 76 (1.32%)	
occurrences (all)	5	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 75 (1.33%)	3 / 76 (3.95%)	
occurrences (all)	1	3	

Dyspepsia			
subjects affected / exposed	1 / 75 (1.33%)	3 / 76 (3.95%)	
occurrences (all)	1	3	
Nausea			
subjects affected / exposed	0 / 75 (0.00%)	4 / 76 (5.26%)	
occurrences (all)	0	4	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 75 (1.33%)	1 / 76 (1.32%)	
occurrences (all)	1	1	
Infections and infestations			
COVID-19			
subjects affected / exposed	7 / 75 (9.33%)	5 / 76 (6.58%)	
occurrences (all)	7	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 June 2022	Amendment 4: The purpose of the amendment was to update the Sponsor's entity name and address change.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported