Clinical trial results:
A Double-Blind, Placebo-Controlled Phase 2b Study to Evaluate the Efficacy and Safety of ARO-APOC3 in Adults with Severe Hypertriglyceridemia

Summary

EudraCT number	2021-000687-30
Trial protocol	DE HU NL PL
Global end of trial date	31 August 2023

Results information

Result version number	v1 (current)
This version publication date	04 September 2024
First version publication date	04 September 2024

Trial information

Trial identification

Sponsor protocol code	AROAPOC3-2001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04720534
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Arrowhead Pharmaceuticals, Inc.
Sponsor organisation address	177 East Colorado Boulevard, Suite 700, Pasadena, CA, United States, 91105
Public contact	Chief Operating Officer,, Arrowhead Pharmaceuticals, Inc., +1 6263043400, info@arrowheadpharma.com
Scientific contact	Chief Operating Officer,, Arrowhead Pharmaceuticals, Inc., +1 6263043400, info@arrowheadpharma.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	31 August 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 August 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate the safety and efficacy of ARO-APOC3 in adults with Severe Hypertriglyceridemia (SHTG) and to select a dosing regimen for later stage clinical studies in this patient population.

Protection of trial subjects:

All eligible participants will have the study explained by the PI or designee. They will receive a full explanation, in lay terms, of the aims of the study, the discomforts, risks and benefits in taking part as well as of insurance and other procedures for compensation in case of injury. It will be explained that the study is for research purposes only and is not expected to provide any therapeutic benefit to the individual. It will be pointed out that they can withdraw from the study at any time without prejudice.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 April 2021
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	Australia: 33
Country: Number of subjects enrolled	Canada: 24
Country: Number of subjects enrolled	New Zealand: 9
Country: Number of subjects enrolled	United States: 89
Country: Number of subjects enrolled	Netherlands: 7
Country: Number of subjects enrolled	Poland: 13
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Hungary: 53
Worldwide total number of subjects	229
EEA total number of subjects	74

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)	187
From 65 to 84 years	42
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

There were 76 study centers in 8 countries (Australia, Canada, Germany, Hungary, The Netherlands, New Zealand, Poland, and the United States [US]).

Pre-assignment

Screening details:

Subjects who met all the protocol eligibility criteria during Screening were enrolled and randomly assigned to treatment in a double-blind fashion. Subjects were randomly assigned 3:1 to receive 1 of 3 ARO-APOC3 dosing regimens (ARO-APOC3 10 mg, 25 mg, or 50 mg) or matched placebo.

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, Monitor

Blinding implementation details:

Treatment assignment (active vs placebo) is blinded in this clinical study. Dose group assignment is not blinded, due to required injection volume differences dictated by the respective dose group. Therefore, during the Double Blind Treatment Period, participants will receive an injection of either active or placebo volume matched to the assigned dose group.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received a total of 2 placebo SC injections on Day 1 and Week 12 for a total of 2 injections.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Each dose of placebo (normal saline 0.9%), will be administered by SC injection by the Investigator or appropriately trained and qualified clinical staff designated by the Investigator.

Arm title	ARO-APOC3 10 mg

Arm description:

Participants received a total of 2 ARO-APOC3 10 mg SC injections on Day 1 and Week 12 for a total of 2 injections.

Arm type	Experimental
Investigational medicinal product name	ARO-APOC3 Injection
Investigational medicinal product code	ARO-APOC3
Other name	plozasiran
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Each dose of active drug (ARO-ANG3) will be administered by SC injection by the Investigator or appropriately trained and qualified clinical staff designated by the Investigator.

Arm title	ARO-APOC3 25 mg

Arm description:

Participants received a total of 2 ARO-APOC3 25 mg SC injections on Day 1 and Week 12 for a total of 2 injections.

Arm type	Experimental
Investigational medicinal product name	ARO-APOC3 Injection
Investigational medicinal product code	ARO-APOC3
Other name	plozasiran
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Each dose of active drug (ARO-ANG3) will be administered by SC injection by the Investigator or appropriately trained and qualified clinical staff designated by the Investigator.

Arm title	ARO-APOC3 50 mg

Arm description:

Participants received a total of 2 ARO-APOC3 50 mg SC injections on Day 1 and Week 12 for a total of 2 injections.

Arm type	Experimental
Investigational medicinal product name	ARO-APOC3 Injection
Investigational medicinal product code	ARO-APOC3
Other name	plozasiran
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Each dose of active drug (ARO-ANG3) will be administered by SC injection by the Investigator or appropriately trained and qualified clinical staff designated by the Investigator.

Number of subjects in period 1	Placebo	ARO-APOC3 10 mg	ARO-APOC3 25 mg
Started	62	55	55
Completed	58	50	52
Not completed	4	5	3
Consent withdrawn by subject	3	1	1
Physician decision	-	-	-
Other, not specified	-	2	-
Adverse event	-	1	-
Lost to follow-up	1	1	2

Number of subjects in period 1	ARO-APOC3 50 mg
Started	57
Completed	53
Not completed	4
Consent withdrawn by subject	1
Physician decision	1
Other, not specified	1
Adverse event	1
Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received a total of 2 placebo SC injections on Day 1 and Week 12 for a total of 2 injections.	
Reporting group title	ARO-APOC3 10 mg
Reporting group description:	
Participants received a total of 2 ARO-APOC3 10 mg SC injections on Day 1 and Week 12 for a total of 2 injections.	
Reporting group title	ARO-APOC3 25 mg
Reporting group description:	
Participants received a total of 2 ARO-APOC3 25 mg SC injections on Day 1 and Week 12 for a total of 2 injections.	
Reporting group title	ARO-APOC3 50 mg
Reporting group description:	
Participants received a total of 2 ARO-APOC3 50 mg SC injections on Day 1 and Week 12 for a total of 2 injections.	

Reporting group values	Placebo	ARO-APOC3 10 mg	ARO-APOC3 25 mg
Number of subjects	62	55	55
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	55.8	52.9	56.0
standard deviation	± 11.22	± 9.55	± 10.64
Gender categorical Units: Subjects			
Female	15	8	12
Male	47	47	43
Race Units: Subjects			
White	56	48	48
Black or African American	1	2	3
American Indian or Alaska Native	1	0	0
Asian	3	1	2
Native Hawaiian or Other Pacific Islander	0	0	2
Unknown	0	1	0
Other, Not Specified	1	3	0
Ethnicity Units: Subjects			
Hispanic or Latino	13	7	7
Not Hispanic or Latino	48	47	48
Not Reported	1	1	0

Reporting group values	ARO-APOC3 50 mg	Total	
Number of subjects	57	229	

Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	54.3		
standard deviation	± 11.00	-	
Gender categorical Units: Subjects			
Female	16	51	
Male	41	178	
Race Units: Subjects			
White	53	205	
Black or African American	1	7	
American Indian or Alaska Native	0	1	
Asian	3	9	
Native Hawaiian or Other Pacific Islander	0	2	
Unknown	0	1	
Other, Not Specified	0	4	
Ethnicity Units: Subjects			
Hispanic or Latino	6	33	
Not Hispanic or Latino	51	194	
Not Reported	0	2	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received a total of 2 placebo SC injections on Day 1 and Week 12 for a total of 2 injections.	
Reporting group title	ARO-APOC3 10 mg
Reporting group description:	
Participants received a total of 2 ARO-APOC3 10 mg SC injections on Day 1 and Week 12 for a total of 2 injections.	
Reporting group title	ARO-APOC3 25 mg
Reporting group description:	
Participants received a total of 2 ARO-APOC3 25 mg SC injections on Day 1 and Week 12 for a total of 2 injections.	
Reporting group title	ARO-APOC3 50 mg
Reporting group description:	
Participants received a total of 2 ARO-APOC3 50 mg SC injections on Day 1 and Week 12 for a total of 2 injections.	

Primary: Percent Change From Baseline at Week 24 in Fasting TG

End point title	Percent Change From Baseline at Week 24 in Fasting TG
End point description:	
Full Analysis Set: All randomized participants who receive at least 1 dose of investigational product (IP). Observed cases.	
End point type	Primary
End point timeframe:	
Baseline, Week 24	

End point values	Placebo	ARO-APOC3 10 mg	ARO-APOC3 25 mg	ARO-APOC3 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	50	54	55
Units: percentage change				
least squares mean (standard error)	-17.2 (± 5.27)	-66.0 (± 5.61)	-70.2 (± 5.51)	-74.2 (± 5.44)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ARO-APOC3 10 mg

Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [1]
Method	Mixed models repeated measures (MMRM)
Parameter estimate	Difference
Point estimate	-48.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-64
upper limit	-33.7

Notes:

[1] - MMRM model includes treatment arm, study visit, and baseline value as model terms. The model also includes treatment by visit and treatment by baseline as interaction terms. Observed cases of the data from baseline through Week 48 are included.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ARO-APOC3 25 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [2]
Method	Mixed models repeated measures (MMRM)
Parameter estimate	Difference
Point estimate	-53.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-68.1
upper limit	-38

Notes:

[2] - MMRM model includes treatment arm, study visit, and baseline value as model terms. The model also includes treatment by visit and treatment by baseline as interaction terms. Observed cases of the data from baseline through Week 48 are included.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ARO-APOC3 50 mg
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [3]
Method	Mixed models repeated measures (MMRM)
Parameter estimate	Difference
Point estimate	-57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-71.9
upper limit	-42.1

Notes:

[3] - MMRM model includes treatment arm, study visit, and baseline value as model terms. The model also includes treatment by visit and treatment by baseline as interaction terms. Observed cases of the data from baseline through Week 48 are included.

Secondary: Percent Change From Baseline Over Time Through Week 48 in Fasting TG

End point title	Percent Change From Baseline Over Time Through Week 48 in Fasting TG

End point description:

Full Analysis Set: All randomized participants who receive at least 1 dose of investigational product (IP). n=Observed cases at given time point.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 36, 48/early termination (ET)

End point values	Placebo	ARO-APOC3 10 mg	ARO-APOC3 25 mg	ARO-APOC3 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	54	55	57
Units: percentage change				
least squares mean (standard error)				
Week 4; n=60, 53, 55, 57	7.2 (± 4.61)	-63.3 (± 4.88)	-79.5 (± 4.81)	-77.6 (± 4.72)
Week 8; n=60, 54, 54, 56	-0.7 (± 5.19)	-54.0 (± 5.46)	-73.2 (± 5.45)	-72.8 (± 5.34)
Week 12; n=57, 53, 54, 54	-7.3 (± 7.05)	-53.9 (± 7.35)	-64.9 (± 7.29)	-70.3 (± 7.24)
Week 16; n=59, 50, 54, 53	-2.9 (± 5.91)	-70.5 (± 6.32)	-80.1 (± 6.17)	-76.3 (± 6.15)
Week 20; n=58, 51, 51, 53	2.4 (± 6.66)	-67.7 (± 7.07)	-75.3 (± 7.02)	-75.6 (± 6.91)
Week 24; n=59, 50, 54, 55	-17.2 (± 5.27)	-66.0 (± 5.61)	-70.2 (± 5.51)	-74.2 (± 5.44)
Week 28; n=60, 50, 52, 54	-11.7 (± 5.83)	-60.0 (± 6.33)	-70.3 (± 6.23)	-70.8 (± 6.11)
Week 36; n=57, 49, 51, 54	-7.6 (± 9.08)	-37.7 (± 9.70)	-64.0 (± 9.54)	-53.6 (± 9.35)
Week 48; n=57, 50, 50, 53	-6.6 (± 7.71)	-31.4 (± 8.20)	-58.0 (± 8.15)	-53.4 (± 7.97)

Attachments (see zip file)	Statistical Analyses-Percent Change from Baseline Over Time

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline at Week 24 in Apolipoprotein (Apo)C-III

End point title	Percent Change From Baseline at Week 24 in Apolipoprotein (Apo)C-III

End point description:

Full Analysis Set: All randomized participants who receive at least 1 dose of investigational product (IP). Observed cases.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Placebo	ARO-APOC3 10 mg	ARO-APOC3 25 mg	ARO-APOC3 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	49	54	55
Units: percentage change				
least squares mean (standard error)	114.2 (± 73.08)	-69.6 (± 76.90)	-73.7 (± 76.04)	-79.4 (± 73.19)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ARO-APOC3 10 mg
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.076 [4]
Method	MMRM
Parameter estimate	Difference
Point estimate	-183.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-387
upper limit	19.4

Notes:

[4] - MMRM model includes treatment arm, study visit, stratification factor, and baseline value as model terms. The model also includes treatment by visit and treatment by baseline as interaction terms.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ARO-APOC3 25 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0677 [5]
Method	MMRM
Parameter estimate	Difference
Point estimate	-187.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-389.6
upper limit	13.8

Notes:

[5] - MMRM model includes treatment arm, study visit, stratification factor, and baseline value as model terms. The model also includes treatment by visit and treatment by baseline as interaction terms.

Statistical analysis title	Statistical Analysis 3

Comparison groups	Placebo v ARO-APOC3 50 mg
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0568 [6]
Method	MMRM
Parameter estimate	Difference
Point estimate	-193.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-392.9
upper limit	5.6

Notes:

[6] - MMRM model includes treatment arm, study visit, stratification factor, and baseline value as model terms. The model also includes treatment by visit and treatment by baseline as interaction terms.

Secondary: Percent Change From Baseline Over Time Through Week 48 in Apolipoprotein (Apo)C-III

End point title	Percent Change From Baseline Over Time Through Week 48 in Apolipoprotein (Apo)C-III

End point description:

Full Analysis Set: All randomized participants who receive at least 1 dose of investigational product (IP). n=Observed cases at given time point.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 36, 48/early termination (ET)

End point values	Placebo	ARO-APOC3 10 mg	ARO-APOC3 25 mg	ARO-APOC3 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	54	55	57
Units: percentage change				
least squares mean (standard error)				
Week 4; n=60, 52, 55, 57	209.3 (± 73.06)	-67.3 (± 76.79)	-84.4 (± 76.00)	-84.6 (± 73.12)
Week 8; n=60, 53, 54, 56	146.3 (± 73.06)	-59.8 (± 76.76)	-78.8 (± 76.03)	-79.9 (± 73.14)
Week 12; n=57, 52, 54, 54	122.2 (± 73.13)	-55.5 (± 76.79)	-71.8 (± 76.04)	-73.2 (± 73.21)
Week 16; n=59, 49, 54, 53	134.4 (± 73.09)	-77.1 (± 76.90)	-86.4 (± 76.04)	-87.1 (± 73.25)
Week 20; n=58, 50, 51, 53	118.8 (± 73.11)	-71.7 (± 76.87)	-81.2 (± 76.13)	-84.0 (± 73.26)
Week 24; n=59, 49, 54, 55	114.2 (± 73.08)	-69.6 (± 76.90)	-73.7 (± 76.04)	-79.4 (± 73.19)
Week 28; n=60, 49, 52, 54	140.2 (± 73.06)	-64.4 (± 76.89)	-71.9 (± 76.09)	-74.7 (± 73.21)
Week 36; n=57, 48, 51, 54	152.0 (± 73.13)	-50.2 (± 76.92)	-60.9 (± 76.12)	-59.9 (± 73.21)
Week 48; n=57, 49, 50, 53	135.8 (± 73.14)	-34.5 (± 76.89)	-49.6 (± 76.16)	-48.3 (± 73.25)

Attachments (see zip file)	Statistical Analyses-Percent Change from Baseline at Week 24

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline at Week 24 in Fasting Non-High-Density Lipoprotein Cholesterol (non-HDL-C)

End point title	Percent Change From Baseline at Week 24 in Fasting Non-High-Density Lipoprotein Cholesterol (non-HDL-C)

End point description:

Full Analysis Set: All randomized participants who receive at least 1 dose of investigational product (IP). Observed cases.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Placebo	ARO-APOC3 10 mg	ARO-APOC3 25 mg	ARO-APOC3 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	49	54	55
Units: percentage change				
least squares mean (standard error)	-1.5 (± 3.76)	-29.4 (± 4.04)	-28.4 (± 3.90)	-21.7 (± 3.83)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ARO-APOC3 10 mg
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [7]
Method	MMRM
Parameter estimate	Difference
Point estimate	-27.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-38.6
upper limit	-17.2

Notes:

[7] - MMRM model includes treatment arm, study visit, stratification factor, and baseline value as model terms. The model also includes treatment by visit and treatment by baseline as interaction terms.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ARO-APOC3 25 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [8]
Method	MMRM
Parameter estimate	Difference
Point estimate	-26.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-37.4
upper limit	-16.4

Notes:

[8] - MMRM model includes treatment arm, study visit, stratification factor, and baseline value as model terms. The model also includes treatment by visit and treatment by baseline as interaction terms.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ARO-APOC3 50 mg
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002 [9]
Method	MMRM
Parameter estimate	Difference
Point estimate	-20.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.6
upper limit	-9.7

Notes:

[9] - MMRM model includes treatment arm, study visit, stratification factor, and baseline value as model terms. The model also includes treatment by visit and treatment by baseline as interaction terms.

Secondary: Percent Change From Baseline Over Time Through Week 48 in Fasting Non-High-Density Lipoprotein Cholesterol (non-HDL-C)

End point title	Percent Change From Baseline Over Time Through Week 48 in Fasting Non-High-Density Lipoprotein Cholesterol (non-HDL-C)

End point description:

Full Analysis Set: All randomized participants who receive at least 1 dose of investigational product (IP). n=Observed cases at given time point.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 36, 48/early termination (ET)

End point values	Placebo	ARO-APOC3 10 mg	ARO-APOC3 25 mg	ARO-APOC3 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	54	55	57
Units: percentage change				
least squares mean (standard error)				
Week 4; n=60, 52, 55, 57	6.3 (± 3.35)	-27.0 (± 3.57)	-34.7 (± 3.46)	-26.1 (± 3.37)
Week 8; n=60, 53, 54, 56	4.5 (± 3.77)	-19.7 (± 4.00)	-30.7 (± 3.92)	-20.7 (± 3.82)
Week 12; n=57, 52, 54, 54	1.4 (± 4.54)	-19.3 (± 4.77)	-30.0 (± 4.67)	-22.3 (± 4.61)
Week 16; n=59, 49, 54, 53	1.8 (± 3.73)	-27.9 (± 4.00)	-37.8 (± 3.87)	-23.7 (± 3.81)
Week 20; n=58, 50, 51, 53	5.7 (± 3.96)	-26.7 (± 4.22)	-34.6 (± 4.13)	-22.9 (± 4.04)
Week 24; n=59, 49, 54, 55	-1.5 (± 3.76)	-29.4 (± 4.04)	-28.4 (± 3.90)	-21.7 (± 3.83)
Week 28; n=60, 49, 52, 54	-2.3 (± 3.82)	-27.4 (± 4.14)	-31.3 (± 4.02)	-24.0 (± 3.92)
Week 36; n=57, 48, 51, 54	-0.3 (± 4.57)	-19.2 (± 4.91)	-23.8 (± 4.78)	-13.1 (± 4.65)
Week 48; n=57, 49, 50, 53	0.5 (± 4.58)	-10.0 (± 4.92)	-23.0 (± 4.83)	-13.5 (± 4.69)

Attachments (see zip file)	Statistical Analyses-Percent Change from Baseline at Week 24

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline at Week 24 in Fasting High-Density Lipoprotein Cholesterol (HDL-C)

End point title	Percent Change From Baseline at Week 24 in Fasting High-Density Lipoprotein Cholesterol (HDL-C)

End point description:

Full Analysis Set: All randomized participants who receive at least 1 dose of investigational product (IP). Observed cases.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Placebo	ARO-APOC3 10 mg	ARO-APOC3 25 mg	ARO-APOC3 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	49	54	55
Units: percentage change				
least squares mean (standard error)	10.6 (± 5.87)	54.2 (± 6.32)	62.8 (± 6.09)	67.6 (± 6.00)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ARO-APOC3 10 mg

Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [10]
Method	MMRM
Parameter estimate	Difference
Point estimate	43.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	26.8
upper limit	60.2

Notes:

[10] - MMRM model includes treatment arm, study visit, stratification factor, and baseline value as model terms. The model also includes treatment by visit and treatment by baseline as interaction terms.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ARO-APOC3 25 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [11]
Method	MMRM
Parameter estimate	Difference
Point estimate	52.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	35.8
upper limit	68.6

Notes:

[11] - MMRM model includes treatment arm, study visit, stratification factor, and baseline value as model terms. The model also includes treatment by visit and treatment by baseline as interaction terms.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ARO-APOC3 50 mg
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [12]
Method	MMRM
Parameter estimate	Difference
Point estimate	57
Confidence interval	
level	95 %
sides	2-sided
lower limit	40.7
upper limit	73.3

Notes:

[12] - MMRM model includes treatment arm, study visit, stratification factor, and baseline value as model terms. The model also includes treatment by visit and treatment by baseline as interaction terms.

Secondary: Percent Change From Baseline Over Time Through Week 48 in Fasting

High-Density Lipoprotein Cholesterol (HDL-C)

End point title	Percent Change From Baseline Over Time Through Week 48 in Fasting High-Density Lipoprotein Cholesterol (HDL-C)

End point description:

Full Analysis Set: All randomized participants who receive at least 1 dose of investigational product (IP). n=Participants with an assessment at given time point.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 36, 48/early termination (ET)

End point values	Placebo	ARO-APOC3 10 mg	ARO-APOC3 25 mg	ARO-APOC3 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	54	55	57
Units: percentage change				
least squares mean (standard error)				
Week 4; n=60, 52, 55, 57	4.3 (± 5.48)	53.4 (± 5.86)	76.2 (± 5.67)	88.1 (± 5.56)
Week 8; n=60, 53, 54, 56	6.2 (± 5.45)	45.4 (± 5.79)	73.5 (± 5.66)	67.7 (± 5.54)
Week 12; n=57, 52, 54, 54	11.3 (± 5.50)	39.9 (± 5.81)	60.2 (± 5.66)	62.5 (± 5.59)
Week 16; n=59, 49, 54, 53	5.7 (± 5.78)	66.2 (± 6.23)	87.1 (± 5.99)	82.6 (± 5.94)
Week 20; n=58, 50, 51, 53	8.8 (± 6.20)	61.2 (± 6.63)	78.7 (± 6.48)	81.2 (± 6.36)
Week 24; n=59, 49, 54, 55	10.6 (± 5.87)	54.2 (± 6.32)	62.8 (± 6.09)	67.6 (± 6.00)
Week 28; n=60, 49, 52, 54	10.2 (± 5.55)	48.2 (± 6.00)	67.2 (± 5.81)	68.0 (± 5.70)
Week 36; n=57, 48, 51, 54	11.7 (± 5.83)	34.5 (± 6.29)	51.1 (± 6.09)	47.2 (± 5.95)
Week 48; n=57, 49, 50, 53	6.1 (± 5.40)	23.5 (± 5.80)	32.4 (± 5.65)	37.8 (± 5.51)

Attachments (see zip file)	Statistical Analyses-Percent Change from Baseline at Week 24

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline at Week 24 in Fasting Total Apolipoprotein B (ApoB)

End point title	Percent Change From Baseline at Week 24 in Fasting Total Apolipoprotein B (ApoB)

End point description:

Full Analysis Set: All randomized participants who receive at least 1 dose of investigational product (IP). Participants with an assessment at given time point.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Placebo	ARO-APOC3 10 mg	ARO-APOC3 25 mg	ARO-APOC3 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	49	54	55
Units: percentage change				
least squares mean (standard error)	8.0 (± 5.85)	6.0 (± 6.31)	-5.3 (± 6.06)	0.7 (± 6.01)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ARO-APOC3 10 mg
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8155 [13]
Method	MMRM
Parameter estimate	Difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.8
upper limit	14.8

Notes:

[13] - MMRM model includes treatment arm, study visit, stratification factor, and baseline value as model terms. The model also includes treatment by visit and treatment by baseline as interaction terms.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ARO-APOC3 25 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1124 [14]
Method	MMRM
Parameter estimate	Difference
Point estimate	-13.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.8
upper limit	3.2

Notes:

[14] - MMRM model includes treatment arm, study visit, stratification factor, and baseline value as model terms. The model also includes treatment by visit and treatment by baseline as interaction terms.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ARO-APOC3 50 mg

Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3791 [15]
Method	MMRM
Parameter estimate	Difference
Point estimate	-7.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.8
upper limit	9.1

Notes:

[15] - MMRM model includes treatment arm, study visit, stratification factor, and baseline value as model terms. The model also includes treatment by visit and treatment by baseline as interaction terms.

Secondary: Percent Change From Baseline Over Time Through Week 48 in Fasting Total Apolipoprotein B (ApoB)

End point title	Percent Change From Baseline Over Time Through Week 48 in Fasting Total Apolipoprotein B (ApoB)

End point description:

Full Analysis Set: All randomized participants who receive at least 1 dose of investigational product (IP). n=Participants with an assessment at given time point.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 36, 48/early termination (ET)

End point values	Placebo	ARO-APOC3 10 mg	ARO-APOC3 25 mg	ARO-APOC3 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	54	55	57
Units: percentage change				
least squares mean (standard error)				
Week 4; n=60, 52, 55, 57	16.2 (± 6.70)	-2.3 (± 7.10)	-9.0 (± 6.95)	-1.9 (± 6.84)
Week 8; n=60, 53, 54, 56	16.0 (± 4.74)	-0.8 (± 4.97)	-7.2 (± 4.89)	1.5 (± 4.82)
Week 12; n=57, 52, 54, 54	4.2 (± 3.70)	0.5 (± 3.80)	-11.2 (± 3.74)	-1.3 (± 3.73)
Week 16; n=59, 49, 54, 53	5.3 (± 4.13)	-0.8 (± 4.34)	-13.1 (± 4.22)	-0.6 (± 4.20)
Week 20; n=58, 50, 51, 53	1.6 (± 3.98)	-0.7 (± 4.17)	-10.3 (± 4.10)	4.4 (± 4.06)
Week 24; n=59, 49, 54, 55	8.0 (± 5.85)	6.0 (± 6.31)	-5.3 (± 6.06)	0.7 (± 6.01)
Week 28; n=60, 49, 52, 54	3.9 (± 3.70)	-1.3 (± 3.92)	-6.0 (± 3.83)	0.6 (± 3.79)
Week 36; n=57, 48, 51, 54	8.9 (± 4.10)	-0.4 (± 4.35)	2.5 (± 4.24)	8.5 (± 4.17)
Week 48; n=57, 49, 50, 53	5.7 (± 4.06)	6.4 (± 4.28)	-0.2 (± 4.21)	2.4 (± 4.14)

Attachments (see zip file)	Statistical Analyses-Percent Change from Baseline at Week 24

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline at Week 24 in Fasting Low-Density Lipoprotein-Cholesterol (LDL-C)

End point title	Percent Change From Baseline at Week 24 in Fasting Low-Density Lipoprotein-Cholesterol (LDL-C)

End point description:

LDL-C analyses used both Martin-Hopkins methodology and ultracentrifugation.

Full Analysis Set: All randomized participants who receive at least 1 dose of investigational product (IP). n=participants with given assessment at given time point.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Placebo	ARO-APOC3 10 mg	ARO-APOC3 25 mg	ARO-APOC3 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	54	55	57
Units: percentage change				
least squares mean (standard error)				
Martin-Hopkins methodology; n=53, 44, 52, 50	-5.5 (± 123.7)	301.9 (± 128.17)	-15.4 (± 120.30)	2.0 (± 123.04)
Ultracentrifugation; n=58, 49, 54, 55	18.0 (± 10.48)	49.0 (± 11.06)	43.7 (± 10.76)	78.2 (± 10.60)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Martin-Hopkins methodology

Comparison groups	Placebo v ARO-APOC3 10 mg
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0737 [16]
Method	MMRM
Parameter estimate	Difference
Point estimate	307.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.8
upper limit	644.6

Notes:

[16] - MMRM model includes treatment arm, study visit, stratification factor, and baseline value as model terms. The model also includes treatment by visit and treatment by baseline as interaction terms.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:	
Martin-Hopkins methodology	
Comparison groups	Placebo v ARO-APOC3 25 mg
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9525 [17]
Method	MMRM
Parameter estimate	Difference
Point estimate	-9.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-337.4
upper limit	317.6

Notes:

[17] - MMRM model includes treatment arm, study visit, stratification factor, and baseline value as model terms. The model also includes treatment by visit and treatment by baseline as interaction terms.

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
Martin-Hopkins methodology	
Comparison groups	Placebo v ARO-APOC3 50 mg
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9644 [18]
Method	MMRM
Parameter estimate	Difference
Point estimate	7.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-323.3
upper limit	338.3

Notes:

[18] - MMRM model includes treatment arm, study visit, stratification factor, and baseline value as model terms. The model also includes treatment by visit and treatment by baseline as interaction terms.

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v ARO-APOC3 10 mg
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0395 [19]
Method	MMRM
Parameter estimate	Difference
Point estimate	31

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.5
upper limit	60.6

Notes:

[19] - MMRM model includes treatment arm, study visit, stratification factor, and baseline value as model terms. The model also includes treatment by visit and treatment by baseline as interaction terms.

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo v ARO-APOC3 25 mg
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0825 [20]
Method	MMRM
Parameter estimate	Difference
Point estimate	25.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	54.9

Notes:

[20] - MMRM model includes treatment arm, study visit, stratification factor, and baseline value as model terms. The model also includes treatment by visit and treatment by baseline as interaction terms.

Statistical analysis title	Statistical Analysis 6
Comparison groups	Placebo v ARO-APOC3 50 mg
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [21]
Method	MMRM
Parameter estimate	Difference
Point estimate	60.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	31.3
upper limit	89.2

Notes:

[21] - MMRM model includes treatment arm, study visit, stratification factor, and baseline value as model terms. The model also includes treatment by visit and treatment by baseline as interaction terms.

Secondary: Percent Change From Baseline Over Time Through Week 48 in Fasting Low-Density Lipoprotein-Cholesterol (LDL-C)

End point title	Percent Change From Baseline Over Time Through Week 48 in Fasting Low-Density Lipoprotein-Cholesterol (LDL-C)

End point description:

LDL-C analyses used both Martin-Hopkins methodology (MHM) and ultracentrifugation (UC).

Full Analysis Set: All randomized participants who receive at least 1 dose of investigational product (IP). n=Participants with given assessment at given time point.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 36, 48/early termination (ET)

End point values	Placebo	ARO-APOC3 10 mg	ARO-APOC3 25 mg	ARO-APOC3 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	54	55	57
Units: percentage change				
least squares mean (standard error)				
MHM Week 4; n=50, 46, 53, 51	-29.3 (± 123.78)	267.3 (± 128.13)	-13.5 (± 120.28)	0.6 (± 123.00)
MHM Week 8; n=52, 47, 51, 49	-11.3 (± 123.74)	297.4 (± 128.11)	-11.7 (± 120.29)	5.3 (± 123.01)
MHM Week 12; n=48, 46, 52, 49	-13.6 (± 123.75)	300.7 (± 128.12)	-17.3 (± 120.29)	3.2 (± 123.02)
MHM Week 16; n=50, 44, 52, 47	-14.3 (± 123.72)	340.3 (± 128.15)	-20.4 (± 120.29)	5.6 (± 123.04)
MHM Week 20; n=48, 45, 49, 48	-7.3 (± 123.72)	306.7 (± 128.15)	-17.4 (± 120.31)	4.9 (± 123.05)
MHM Week 24; n=53, 44, 52, 50	-5.5 (± 123.67)	301.9 (± 128.17)	-15.4 (± 120.30)	2.0 (± 123.04)
MHM Week 28; n=52, 44, 50, 49	-12.1 (± 123.68)	283.2 (± 128.20)	-12.1 (± 120.34)	-4.7 (± 123.06)
MHM Week 36; n=48, 42, 49, 47	-5.5 (± 123.73)	254.7 (± 128.28)	-0.7 (± 120.38)	1.6 (± 123.10)
MHM Week 48; n=50, 43, 48, 48	-11.5 (± 123.77)	286.5 (± 128.34)	-9.0 (± 120.44)	-5.3 (± 123.12)
UC Week 4; n=59, 52, 55, 57	4.4 (± 9.65)	50.3 (± 10.10)	47.3 (± 9.88)	69.1 (± 9.67)
UC Week 8; n=59, 53, 54, 56	15.8 (± 10.44)	49.8 (± 10.92)	45.8 (± 10.73)	65.4 (± 10.51)
UC Week 12; n=55, 52, 53, 53	17.1 (± 10.17)	50.9 (± 10.57)	36.0 (± 10.38)	65.8 (± 10.22)
UC Week 16; n=57, 49, 54, 53	19.3 (± 12.14)	62.6 (± 12.80)	41.7 (± 12.46)	87.1 (± 12.31)
UC Week 20; n=56, 50, 50, 53	16.8 (± 11.79)	62.7 (± 12.38)	42.3 (± 12.16)	85.9 (± 11.93)
UC Week 24; n=58, 49, 54, 55	18.0 (± 10.48)	49.0 (± 11.06)	43.7 (± 10.76)	78.2 (± 10.60)
UC Week 28; n=59, 49, 51, 54	15.4 (± 10.14)	50.8 (± 10.76)	42.3 (± 10.51)	61.6 (± 10.30)
UC Week 36; n=56, 48, 51, 54	18.4 (± 9.89)	35.5 (± 10.47)	51.5 (± 10.20)	61.3 (± 9.97)
UC Week 48; n=56, 49, 50, 53	21.3 (± 10.73)	33.5 (± 11.36)	34.4 (± 11.14)	44.6 (± 10.87)

Attachments (see zip file)	Statistical Analyses-Percent Change from Baseline at Week 24 Statistical Analyses - Percent Change from Baseline at Week 24

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Plasma Concentrations of ARO-APOC3 Over TimeThrough Week 12

End point title	Change From Baseline in Plasma Concentrations of ARO-APOC3 Over TimeThrough Week 12[22]

End point description:

Full PK Analysis Set: Full Analysis Set (FAS) participants (all randomized participants who receive at least 1 dose of IP during the study period) who have sufficient plasma concentration data to facilitate determination of PK parameters.

End point type	Secondary

End point timeframe:

Day 1: pre-dose, 15 minutes, 1, 3, 6, 24 hours post-dose; Week 12: pre-dose, 15 minutes, 1, 3, 6, 24 hours post-dose

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: Per protocol, placebo arm was not analyzed for this measure.

End point values	ARO-APOC3 10 mg	ARO-APOC3 25 mg	ARO-APOC3 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	9	10	
Units: ng/mL				
arithmetic mean (standard deviation)				
Day 1, Pre-Dose; n=9, 9, 9	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)	
Day 1, 15 Minutes Post-Dose; n=9, 9, 8	10.258 (± 12.4741)	21.207 (± 21.7982)	34.352 (± 27.3986)	
Day 1, 1 Hour Post-Dose; n=9, 8, 9	18.124 (± 18.1760)	37.396 (± 27.9849)	58.508 (± 29.0222)	
Day 1, 3 Hours Post-Dose; n=9, 8, 9	20.217 (± 16.8127)	50.596 (± 53.3270)	58.493 (± 30.5510)	
Day 1, 6 Hours Post-Dose; n=9, 7, 9	17.147 (± 14.6145)	51.813 (± 44.2610)	64.019 (± 26.3749)	
Day 1, 24 Hours Post-Dose; n=9, 6, 9	7.921 (± 16.9181)	10.316 (± 11.5852)	11.587 (± 6.4288)	
Week 12, Pre-Dose; n=8, 8, 10	0.000 (± 0.0000)	0.000 (± 0.0000)	0.000 (± 0.0000)	
Week 12, 15 Minutes Post-Dose; n=8, 7, 10	10.188 (± 9.4024)	23.576 (± 29.1713)	38.500 (± 32.4047)	
Week 12, 1 Hour Post-Dose; n=8, 8, 10	17.090 (± 12.7636)	35.513 (± 26.5491)	57.939 (± 26.8754)	
Week 12, 3 Hours Post-Dose; n=8, 8, 10	15.101 (± 9.5156)	42.591 (± 39.0808)	65.482 (± 44.5255)	
Week 12, 6 Hours Post-Dose; n=7, 7, 10	11.131 (± 6.6894)	56.230 (± 52.4345)	73.444 (± 42.1339)	
Week 12, 24 Hours Post-Dose; n=8, 7, 10	3.143 (± 5.5271)	6.241 (± 7.5820)	12.125 (± 8.5500)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment-Emergent Adverse Events (TEAEs)

End point title	Number of Participants With Treatment-Emergent Adverse Events (TEAEs)

End point description:

An adverse event (AE) is any untoward medical occurrence, which does not necessarily have to have a causal relationship with this treatment. A serious AE (SAE) is an AE that: results in death; is life-

threatening; requires inpatient hospitalization or prolongation of an existing hospitalization; results in persistent or significant disability/incapacity; is a congenital anomaly/birth defect; or is a medically important event or reaction. TEAEs are AEs that occur following investigational product (IP) administration or a pre-existing condition exacerbated following IP administration.
Safety Analysis Set: All participants who receive at least 1 dose of IP.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	Placebo	ARO-APOC3 10 mg	ARO-APOC3 25 mg	ARO-APOC3 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	54	55	56
Units: participants				
All Treatment-Emergent Adverse Events (TEAEs)	43	43	36	49
Treatment-related TEAEs	8	13	8	10
Serious TEAEs	10	4	2	7
TEAEs leading to study drug discontinuation	0	1	0	0
Deaths	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Post-hoc: Ad Hoc Analysis: Percent Change from Baseline at Week 24 and Over Time Through Week 48 in ApoC-III

End point title	Ad Hoc Analysis: Percent Change from Baseline at Week 24 and Over Time Through Week 48 in ApoC-III

End point description:

Full Analysis Set: All randomized participants who receive at least 1 dose of investigational product (IP), excluding participants with values below the limit of quantification (BLQ) at Baseline, along with one site. n=Observed cases at given time point.

End point type	Post-hoc

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 36, 48/early termination (ET)

End point values	Placebo	ARO-APOC3 10 mg	ARO-APOC3 25 mg	ARO-APOC3 50 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	53	55	57
Units: percentage change				
least squares mean (standard error)				
Week 4; n=57, 51, 55, 57	7.0 (± 3.88)	-65.1 (± 4.04)	-82.9 (± 3.94)	-83.2 (± 3.81)
Week 8; n=57, 52, 54, 56	4.7 (± 4.19)	-57.3 (± 4.36)	-77.2 (± 4.26)	-78.7 (± 4.14)

Week 12; n=54, 51, 54, 54	0.0 (± 4.79)	-53.2 (± 4.97)	-70.3 (± 4.84)	-72.2 (± 4.74)
Week 16; n=56, 49, 54, 53	2.8 (± 3.94)	-74.8 (± 4.13)	-84.9 (± 4.00)	-86.3 (± 3.92)
Week 20; n=56, 50, 51, 53	7.8 (± 4.60)	-69.9 (± 4.81)	-79.7 (± 4.72)	-82.6 (± 4.60)
Week 24; n=56, 48, 54, 55	-0.8 (± 4.29)	-68.1 (± 4.51)	-72.1 (± 4.37)	-78.2 (± 4.26)
Week 28; n=57, 49, 52, 54	-2.2 (± 4.19)	-63.0 (± 4.42)	-70.2 (± 4.31)	-73.2 (± 4.19)
Week 36; n=54, 48, 51, 54	0.2 (± 4.98)	-48.5 (± 5.23)	-59.1 (± 5.10)	-58.3 (± 4.95)
Week 48; n=54, 49, 50, 53	5.6 (± 6.19)	-33.7 (± 6.48)	-48.0 (± 6.37)	-46.8 (± 6.19)

Attachments (see zip file)	Statistical Analyses-Percent Change from Baseline at Week 24

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 48 Weeks	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received a total of 2 placebo SC injections on Day 1 and Week 12 for a total of 2 injections.	
Reporting group title	ARO-APOC3 10 mg
Reporting group description:	
Participants received a total of 2 ARO-APOC3 10 mg SC injections on Day 1 and Week 12 for a total of 2 injections.	
Reporting group title	ARO-APOC3 25 mg
Reporting group description:	
Participants received a total of 2 ARO-APOC3 25 mg SC injections on Day 1 and Week 12 for a total of 2 injections.	
Reporting group title	ARO-APOC3 50 mg
Reporting group description:	
Participants received a total of 2 ARO-APOC3 50 mg SC injections on Day 1 and Week 12 for a total of 2 injections.	

Serious adverse events	Placebo	ARO-APOC3 10 mg	ARO-APOC3 25 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 61 (16.39%)	4 / 54 (7.41%)	2 / 55 (3.64%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer stage III			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (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
Squamous cell carcinoma			

subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (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
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (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
Wrist fracture			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (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
Vascular disorders			
Peripheral artery thrombosis			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (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			
Angina unstable			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (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
Coronary artery disease			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (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
Coronary artery stenosis			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (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
Nervous system disorders			
Cerebrovascular accident			

subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Epilepsy			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (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
Ischaemic stroke			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (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
Abdominal pain			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (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
Enteritis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (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
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (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
Pancreatic pseudocyst			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (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
Pancreatitis necrotising			

subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (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
Pancreatitis relapsing			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
COVID-19			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Nephrolithiasis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (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
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (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
Infections and infestations			
Pneumonia bacterial			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Sepsis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (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	ARO-APOC3 50 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 56 (12.50%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer stage III			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Wrist fracture			

subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Peripheral artery thrombosis			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina unstable			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Coronary artery disease			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Coronary artery stenosis			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Epilepsy			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ischaemic stroke			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enteritis			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatic pseudocyst			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis necrotising			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis relapsing			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19			

subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nephrolithiasis			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia bacterial			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 56 (1.79%)		
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	ARO-APOC3 10 mg	ARO-APOC3 25 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 61 (72.13%)	44 / 54 (81.48%)	36 / 55 (65.45%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	2	0	0
Bowen's disease			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Haemangioma of liver			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Lentigo maligna			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Malignant melanoma			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Uterine leiomyoma			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 61 (6.56%)	0 / 54 (0.00%)	2 / 55 (3.64%)
occurrences (all)	5	0	2
Haematoma			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Hypotension			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Peripheral artery aneurysm			

subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Peripheral artery thrombosis			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	2 / 61 (3.28%)	2 / 54 (3.70%)	1 / 55 (1.82%)
occurrences (all)	2	3	1
Fatigue			
subjects affected / exposed	1 / 61 (1.64%)	2 / 54 (3.70%)	2 / 55 (3.64%)
occurrences (all)	1	2	2
Injection site pain			
subjects affected / exposed	0 / 61 (0.00%)	2 / 54 (3.70%)	2 / 55 (3.64%)
occurrences (all)	0	2	2
Chest pain			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Injection site erythema			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Injection site pruritus			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	2	0	0
Influenza like illness			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Pyrexia			

subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	2	0
Vessel puncture site bruise			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Erectile dysfunction			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 61 (1.64%)	1 / 54 (1.85%)	1 / 55 (1.82%)
occurrences (all)	1	1	2
Epistaxis			
subjects affected / exposed	0 / 61 (0.00%)	2 / 54 (3.70%)	0 / 55 (0.00%)
occurrences (all)	0	2	0
Nasal congestion			
subjects affected / exposed	1 / 61 (1.64%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	1	1	0
Oropharyngeal pain			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	0 / 61 (0.00%)	2 / 54 (3.70%)	0 / 55 (0.00%)
occurrences (all)	0	2	0
Dyspnoea at rest			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Hypoxia			

subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Obstructive sleep apnoea syndrome			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Productive cough			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract congestion			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 61 (1.64%)	1 / 54 (1.85%)	1 / 55 (1.82%)
occurrences (all)	2	1	1
Insomnia			
subjects affected / exposed	1 / 61 (1.64%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	1	1	0
Investigations			
Glycosylated haemoglobin increased			
subjects affected / exposed	2 / 61 (3.28%)	4 / 54 (7.41%)	2 / 55 (3.64%)
occurrences (all)	3	4	2
Lipase increased			
subjects affected / exposed	2 / 61 (3.28%)	2 / 54 (3.70%)	2 / 55 (3.64%)
occurrences (all)	2	2	2
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 61 (1.64%)	1 / 54 (1.85%)	2 / 55 (3.64%)
occurrences (all)	1	1	2
Blood glucose increased			
subjects affected / exposed	0 / 61 (0.00%)	2 / 54 (3.70%)	1 / 55 (1.82%)
occurrences (all)	0	4	1
Amylase increased			
subjects affected / exposed	2 / 61 (3.28%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	2	0	0
Anion gap increased			

subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Blood creatinine increased			
subjects affected / exposed	1 / 61 (1.64%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	1	1	0
Blood insulin increased			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	1 / 55 (1.82%)
occurrences (all)	0	2	1
Blood pressure increased			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	1 / 55 (1.82%)
occurrences (all)	0	1	1
Blood testosterone decreased			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Glucose urine present			
subjects affected / exposed	1 / 61 (1.64%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	1	1	0
Insulin C-peptide increased			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	2	0
Activated partial thromboplastin time abnormal			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	2	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
C-reactive protein increased			

subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Cardiac murmur			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram change			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Globulins decreased			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Glomerular filtration rate decreased			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Haemoglobin decreased			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	2	0
Low density lipoprotein increased			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Occult blood positive			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Platelet count increased			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Protein urine present			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0

Serum ferritin decreased			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Diabetes mellitus			
subjects affected / exposed	2 / 61 (3.28%)	4 / 54 (7.41%)	1 / 55 (1.82%)
occurrences (all)	2	4	1
Hyperuricaemia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 61 (1.64%)	3 / 54 (5.56%)	1 / 55 (1.82%)
occurrences (all)	1	3	1
Muscle strain			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Procedural pain			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	1	0	1
Skin laceration			
subjects affected / exposed	2 / 61 (3.28%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	2	1	0
Contusion			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	1 / 55 (1.82%)
occurrences (all)	0	1	1
Epicondylitis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Exposure to toxic agent			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Graft complication			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Hand fracture			

subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Ligament rupture			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Muscle rupture			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Rib fracture			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Soft tissue injury			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Thermal burn			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Tooth injury			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Traumatic intracranial haemorrhage			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Wrist fracture			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	1	0	1

Atrioventricular block first degree			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Palpitations			
subjects affected / exposed	0 / 61 (0.00%)	2 / 54 (3.70%)	0 / 55 (0.00%)
occurrences (all)	0	2	0
Atrial fibrillation			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Bradycardia			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Bundle branch block left			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Bundle branch block right			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Ventricular extrasystoles			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 61 (4.92%)	8 / 54 (14.81%)	6 / 55 (10.91%)
occurrences (all)	3	10	6
Migraine			
subjects affected / exposed	1 / 61 (1.64%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	1	1	0
Dizziness			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	1	0	1
Hypoaesthesia			
subjects affected / exposed	1 / 61 (1.64%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	1	1	0
Neuropathy peripheral			

subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	1	0	1
Sciatica			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	1 / 55 (1.82%)
occurrences (all)	0	1	1
Carpal tunnel syndrome			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Cervicogenic headache			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Diabetic neuropathy			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Epilepsy			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	2	0	0
Facial paralysis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Hypersomnia			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Lacunar infarction			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Radiculopathy			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	2 / 61 (3.28%)	2 / 54 (3.70%)	0 / 55 (0.00%)
occurrences (all)	2	2	0
Leukocytosis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	1 / 55 (1.82%)
occurrences (all)	0	1	1
Thrombocytopenia			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	1	0	1
Iron deficiency anaemia			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Lymphocytosis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Pancytopenia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Splenomegaly			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Vitreous floaters			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	5 / 61 (8.20%)	3 / 54 (5.56%)	1 / 55 (1.82%)
occurrences (all)	5	3	1
Abdominal pain			
subjects affected / exposed	2 / 61 (3.28%)	2 / 54 (3.70%)	0 / 55 (0.00%)
occurrences (all)	2	2	0
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 61 (4.92%)	2 / 54 (3.70%)	0 / 55 (0.00%)
occurrences (all)	3	2	0
Nausea			
subjects affected / exposed	1 / 61 (1.64%)	2 / 54 (3.70%)	2 / 55 (3.64%)
occurrences (all)	1	2	2
Abdominal pain upper			
subjects affected / exposed	2 / 61 (3.28%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	2	1	0
Haemorrhoids			
subjects affected / exposed	0 / 61 (0.00%)	2 / 54 (3.70%)	1 / 55 (1.82%)
occurrences (all)	0	2	1
Inguinal hernia			
subjects affected / exposed	1 / 61 (1.64%)	1 / 54 (1.85%)	1 / 55 (1.82%)
occurrences (all)	1	1	1
Vomiting			
subjects affected / exposed	1 / 61 (1.64%)	1 / 54 (1.85%)	1 / 55 (1.82%)
occurrences (all)	1	1	1
Abdominal pain lower			
subjects affected / exposed	1 / 61 (1.64%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	1	1	0
Constipation			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Irritable bowel syndrome			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Abdominal tenderness			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	2	0

Diverticulum			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Diverticulum intestinal			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorder			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Hiatus hernia			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Intestinal polyp			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Large intestine polyp			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Vomiting projectile			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	2 / 55 (3.64%)
occurrences (all)	1	0	2
Gallbladder polyp			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Hepatic cyst			

subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Hepatomegaly			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	3 / 55 (5.45%)
occurrences (all)	1	0	3
Dermatitis			
subjects affected / exposed	1 / 61 (1.64%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	1	1	0
Dry skin			
subjects affected / exposed	1 / 61 (1.64%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	1	1	0
Dermatitis allergic			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Dermatitis contact			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Drug eruption			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Hyperhidrosis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Ingrowing nail			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Neuropathic ulcer			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Night sweats			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0

Pruritus			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Rash papular			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Rash pruritic			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Skin discolouration			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	1 / 61 (1.64%)	1 / 54 (1.85%)	1 / 55 (1.82%)
occurrences (all)	1	1	1
Nephrolithiasis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	2 / 55 (3.64%)
occurrences (all)	0	1	2
Chronic kidney disease			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	2 / 55 (3.64%)
occurrences (all)	0	0	2
Renal cyst			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	1 / 55 (1.82%)
occurrences (all)	0	1	1
Calculus urinary			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Dysuria			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Microalbuminuria			

subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Testicular failure			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 61 (8.20%)	3 / 54 (5.56%)	1 / 55 (1.82%)
occurrences (all)	5	3	1
Back pain			
subjects affected / exposed	1 / 61 (1.64%)	5 / 54 (9.26%)	1 / 55 (1.82%)
occurrences (all)	1	5	1
Myalgia			
subjects affected / exposed	1 / 61 (1.64%)	2 / 54 (3.70%)	2 / 55 (3.64%)
occurrences (all)	2	2	2
Musculoskeletal chest pain			
subjects affected / exposed	0 / 61 (0.00%)	2 / 54 (3.70%)	2 / 55 (3.64%)
occurrences (all)	0	2	2
Pain in extremity			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	1 / 55 (1.82%)
occurrences (all)	0	1	1
Osteoarthritis			
subjects affected / exposed	0 / 61 (0.00%)	2 / 54 (3.70%)	0 / 55 (0.00%)
occurrences (all)	0	2	0
Fibromyalgia			
subjects affected / exposed	0 / 61 (0.00%)	2 / 54 (3.70%)	0 / 55 (0.00%)
occurrences (all)	0	2	0
Muscle spasms			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	1 / 55 (1.82%)
occurrences (all)	0	1	1
Muscular weakness			

subjects affected / exposed	0 / 61 (0.00%)	2 / 54 (3.70%)	0 / 55 (0.00%)
occurrences (all)	0	2	0
Neck pain			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Arthritis			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Bursitis			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Intervertebral disc degeneration			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Intervertebral disc protrusion			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Joint effusion			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Joint swelling			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Musculoskeletal pain			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal stiffness			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	2	0	0
Rhabdomyolysis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Rheumatoid arthritis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	2	0
Rotator cuff syndrome			

subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Tendon disorder			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Tenosynovitis stenosans			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	9 / 61 (14.75%)	11 / 54 (20.37%)	9 / 55 (16.36%)
occurrences (all)	10	11	9
Upper respiratory tract infection			
subjects affected / exposed	4 / 61 (6.56%)	5 / 54 (9.26%)	4 / 55 (7.27%)
occurrences (all)	5	6	4
Urinary tract infection			
subjects affected / exposed	6 / 61 (9.84%)	6 / 54 (11.11%)	1 / 55 (1.82%)
occurrences (all)	6	9	2
Bronchitis			
subjects affected / exposed	2 / 61 (3.28%)	4 / 54 (7.41%)	0 / 55 (0.00%)
occurrences (all)	2	4	0
Sinusitis			
subjects affected / exposed	0 / 61 (0.00%)	3 / 54 (5.56%)	4 / 55 (7.27%)
occurrences (all)	0	3	4
Ear infection			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	2 / 61 (3.28%)	1 / 54 (1.85%)	2 / 55 (3.64%)
occurrences (all)	2	1	3
Nasopharyngitis			
subjects affected / exposed	1 / 61 (1.64%)	2 / 54 (3.70%)	0 / 55 (0.00%)
occurrences (all)	1	2	0
Cellulitis			
subjects affected / exposed	1 / 61 (1.64%)	2 / 54 (3.70%)	0 / 55 (0.00%)
occurrences (all)	1	2	0

Tooth infection			
subjects affected / exposed	1 / 61 (1.64%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	1	1	0
Pharyngitis			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	1	0	1
Conjunctivitis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	1 / 55 (1.82%)
occurrences (all)	0	1	1
Cystitis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Lower respiratory tract infection			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Wound infection			
subjects affected / exposed	2 / 61 (3.28%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	2	0	0
Acute sinusitis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Bacterial vulvovaginitis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Coronavirus infection			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Cytomegalovirus colitis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Diverticulitis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0

Eye infection			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Fungal infection			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Gastrointestinal infection			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Hordeolum			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Oral candidiasis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Otitis media			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Periodontitis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Pneumonia fungal			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Respiratory tract infection			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Skin infection			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Subcutaneous abscess			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0

Tonsillitis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Tooth abscess			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	2 / 61 (3.28%)	1 / 54 (1.85%)	1 / 55 (1.82%)
occurrences (all)	2	1	1
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	3 / 61 (4.92%)	1 / 54 (1.85%)	4 / 55 (7.27%)
occurrences (all)	4	1	4
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 61 (0.00%)	2 / 54 (3.70%)	0 / 55 (0.00%)
occurrences (all)	0	2	0
Hypertriglyceridaemia			
subjects affected / exposed	1 / 61 (1.64%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	3	1	0
Hypoglycaemia			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	1	0	1
Vitamin D deficiency			
subjects affected / exposed	1 / 61 (1.64%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	1	1	0
Gout			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			

subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1
Hyperinsulinaemia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Hypernatraemia			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Hyperphosphataemia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Impaired fasting glucose			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Increased appetite			
subjects affected / exposed	1 / 61 (1.64%)	0 / 54 (0.00%)	0 / 55 (0.00%)
occurrences (all)	1	0	0
Iron deficiency			
subjects affected / exposed	0 / 61 (0.00%)	1 / 54 (1.85%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Latent autoimmune diabetes in adults			
subjects affected / exposed	0 / 61 (0.00%)	0 / 54 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1

Non-serious adverse events	ARO-APOC3 50 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	50 / 56 (89.29%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Bowen's disease			

subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Haemangioma of liver subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Lentigo maligna subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Malignant melanoma subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Uterine leiomyoma subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 1		
Vascular disorders			
Hypertension subjects affected / exposed occurrences (all)	5 / 56 (8.93%) 5		
Haematoma subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Hypotension subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Peripheral arterial occlusive disease subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Peripheral artery aneurysm subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Peripheral artery thrombosis subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
General disorders and administration site conditions			

Non-cardiac chest pain subjects affected / exposed occurrences (all)	2 / 56 (3.57%) 2		
Fatigue subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 1		
Injection site pain subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 1		
Chest pain subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 1		
Injection site erythema subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 2		
Injection site pruritus subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 1		
Influenza like illness subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 1		
Malaise subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Oedema peripheral subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Pyrexia subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Vessel puncture site bruise subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Reproductive system and breast disorders			

Benign prostatic hyperplasia			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Erectile dysfunction			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Epistaxis			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Nasal congestion			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Rhinorrhoea			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Sinus congestion			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Dyspnoea at rest			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Hypoxia			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Obstructive sleep apnoea syndrome			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Productive cough			

subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Upper respiratory tract congestion			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Investigations			
Glycosylated haemoglobin increased			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Lipase increased			
subjects affected / exposed	4 / 56 (7.14%)		
occurrences (all)	5		
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Blood glucose increased			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Amylase increased			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Anion gap increased			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Blood creatinine increased			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Blood insulin increased			

subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Blood pressure increased				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Blood testosterone decreased				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences (all)	1			
Glucose urine present				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Insulin C-peptide increased				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences (all)	1			
Activated partial thromboplastin time abnormal				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences (all)	1			
Activated partial thromboplastin time prolonged				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Alanine aminotransferase increased				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences (all)	1			
Aspartate aminotransferase increased				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
C-reactive protein increased				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Cardiac murmur				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences (all)	1			
Electrocardiogram QT prolonged				

subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Electrocardiogram change				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Globulins decreased				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Glomerular filtration rate decreased				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Haemoglobin decreased				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
International normalised ratio increased				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Low density lipoprotein increased				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences (all)	1			
Occult blood positive				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Platelet count increased				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Protein urine present				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences (all)	1			
Serum ferritin decreased				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences (all)	1			
Diabetes mellitus				
subjects affected / exposed	3 / 56 (5.36%)			
occurrences (all)	3			

Hyperuricaemia			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Muscle strain			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Procedural pain			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Skin laceration			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Epicondylitis			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Exposure to toxic agent			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Graft complication			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Hand fracture			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Ligament rupture			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Limb injury			

subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Muscle rupture			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Rib fracture			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Skin abrasion			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Soft tissue injury			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Thermal burn			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Tooth injury			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Traumatic intracranial haemorrhage			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Wrist fracture			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Atrioventricular block first degree			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Palpitations			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		

Atrial fibrillation subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 1			
Bradycardia subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0			
Bundle branch block left subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0			
Bundle branch block right subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 1			
Ventricular extrasystoles subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 1			
Nervous system disorders Headache subjects affected / exposed occurrences (all)	2 / 56 (3.57%) 3			
Migraine subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 1			
Dizziness subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0			
Hypoaesthesia subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0			
Neuropathy peripheral subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0			
Sciatica subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0			
Carpal tunnel syndrome				

subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Cervicogenic headache			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Diabetic neuropathy			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Epilepsy			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Facial paralysis			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Hypersomnia			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Lacunar infarction			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Paraesthesia			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Radiculopathy			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Syncope			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Leukocytosis			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		

Thrombocytopenia subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Iron deficiency anaemia subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Lymphocytosis subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Pancytopenia subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 1		
Splenomegaly subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Ear and labyrinth disorders			
Ear pain subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 1		
Vertigo subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Eye disorders			
Vision blurred subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Vitreous floaters subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Gastrointestinal disorders			
Diarrhoea subjects affected / exposed occurrences (all)	1 / 56 (1.79%) 1		
Abdominal pain subjects affected / exposed occurrences (all)	3 / 56 (5.36%) 3		
Gastrooesophageal reflux disease			

subjects affected / exposed	2 / 56 (3.57%)			
occurrences (all)	2			
Nausea				
subjects affected / exposed	2 / 56 (3.57%)			
occurrences (all)	3			
Abdominal pain upper				
subjects affected / exposed	2 / 56 (3.57%)			
occurrences (all)	2			
Haemorrhoids				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Inguinal hernia				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Vomiting				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Abdominal pain lower				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Constipation				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences (all)	1			
Irritable bowel syndrome				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences (all)	1			
Abdominal tenderness				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Diverticulum				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Diverticulum intestinal				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences (all)	1			
Gastritis				

subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Gastrointestinal disorder			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Hiatus hernia			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Intestinal polyp			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Large intestine polyp			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Toothache			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Vomiting projectile			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Gallbladder polyp			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Hepatic cyst			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Hepatomegaly			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Rash			

subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Dermatitis				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Dry skin				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Dermatitis allergic				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Dermatitis contact				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Drug eruption				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Hyperhidrosis				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences (all)	1			
Ingrowing nail				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Neuropathic ulcer				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Night sweats				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Pruritus				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Rash papular				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Rash pruritic				

subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Skin discolouration			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Nephrolithiasis			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Chronic kidney disease			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Renal cyst			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Calculus urinary			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Dysuria			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Haematuria			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Microalbuminuria			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Testicular failure			

subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 56 (7.14%)		
occurrences (all)	4		
Back pain			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Musculoskeletal chest pain			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Osteoarthritis			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Fibromyalgia			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Muscular weakness			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Neck pain			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	2		
Arthritis			

subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Bursitis				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Intervertebral disc degeneration				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Intervertebral disc protrusion				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Joint effusion				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Joint swelling				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Musculoskeletal pain				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Musculoskeletal stiffness				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Rhabdomyolysis				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences (all)	1			
Rheumatoid arthritis				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Rotator cuff syndrome				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences (all)	1			
Tendon disorder				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Tenosynovitis stenosans				

subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Infections and infestations			
COVID-19			
subjects affected / exposed	9 / 56 (16.07%)		
occurrences (all)	10		
Upper respiratory tract infection			
subjects affected / exposed	7 / 56 (12.50%)		
occurrences (all)	8		
Urinary tract infection			
subjects affected / exposed	4 / 56 (7.14%)		
occurrences (all)	5		
Bronchitis			
subjects affected / exposed	4 / 56 (7.14%)		
occurrences (all)	5		
Sinusitis			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Ear infection			
subjects affected / exposed	4 / 56 (7.14%)		
occurrences (all)	5		
Influenza			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Cellulitis			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	2		
Tooth infection			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Pharyngitis			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		

Conjunctivitis				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Cystitis				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences (all)	1			
Gastroenteritis				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences (all)	1			
Lower respiratory tract infection				
subjects affected / exposed	2 / 56 (3.57%)			
occurrences (all)	2			
Wound infection				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Acute sinusitis				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Bacterial vulvovaginitis				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Coronavirus infection				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Cytomegalovirus colitis				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Diverticulitis				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Eye infection				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Fungal infection				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			

Gastrointestinal infection				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Hordeolum				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Oral candidiasis				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Otitis media				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Periodontitis				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Pneumonia				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Pneumonia fungal				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Respiratory tract infection				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Skin infection				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Subcutaneous abscess				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Tonsillitis				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences (all)	0			
Tooth abscess				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences (all)	1			

Viral infection			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Joint injury			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	6 / 56 (10.71%)		
occurrences (all)	6		
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Hypertriglyceridaemia			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Hypoglycaemia			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Vitamin D deficiency			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Gout			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Hyperglycaemia			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Hyperinsulinaemia			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Hypernatraemia			

subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Hyperphosphataemia			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Hypomagnesaemia			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Impaired fasting glucose			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Increased appetite			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Iron deficiency			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		
Latent autoimmune diabetes in adults			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 January 2021	- Increased the projected number of investigative sites - Revised the Treatment Modification guidelines in subjects with elevated liver function enzymes - Revised inclusion criterion related to prior evidence of triglycerides (TG) ≥ 500 - Revised exclusion criterion related to planned major surgery, coronary interventions, and blood donations - Corrected TG randomization stratification reference timepoint - Clarified clinical events documentation relative to adverse events (AE) assessments - Added a pharmacokinetic (PK) sample collection timepoint at Week 48/end of study (EOS) - Clarified that magnetic resonance imaging -proton density fat fraction (MRI-PDFF) should have been collected as unscheduled visit in case of early termination prior to Week 24 - Clarified that subjects on statin lipid-lowering therapy must have been on an optimal regimen - Revised lipid monitoring thresholds and follow-up procedures - Clarified that the study blind applied to treatment allocation and not to dose group allocation - Clarified that efficacy analysis will include treatment by baseline interaction terms - Revised liver related study modification and follow-up guidelines for subjects with baseline predose evidence of liver disease
19 April 2021	- Data Safety Committee (DSC) recommendations and Treatment Stopping Rules updated to align with the DSC Charter and United States Food and Drug Administration (US FDA) Guidance - Eligibility Criteria updated to add: qualifying mean triglyceride value; defined stable regimen durations for specific background medications; laboratory sign exclusions; exclusion for known genetically confirmed familial chylomicronemia syndrome (FCS) - Clarified Secondary and Exploratory Endpoints - Revised schedule of assessments (SOA) to include three distinct Screening visits and updated fasting requirement to at least 10 hours prior to any lipid testing collection - Revised Lipid Monitoring to provide unblinded low-density lipoprotein cholesterol (LDL-C) values after Week 24 if results cross predefined threshold relative to baseline

01 November 2021	- Updated Sponsor Medical Monitor - Reduction in the total number of subjects to be enrolled - Update to Treatment Stopping Rules - Eligibility Criteria updated - Updated genetic testing panel to include GPD1 mutation associated with FCS - Updates to the SOA - Added Risk-Benefit Analysis - Revised TG monitoring requirements to include only those subjects with a history of acute pancreatitis within 2 years of Day 1 - Added acute pancreatitis events counseling, detection, and reporting requirements - Added an independent pancreatitis adjudication committee - Updates to Laboratory Testing - Clarification that the mean of the two fasting screening values together with the fasting Day 1 TG value was to serve as the baseline value for the primary endpoint analysis - Updated the circumstances under which the Sponsor may have terminated the study - Updated SAE reporting time-frame - Added Data Protection section - Updated Liver Related Study Modification and Follow-Up Guidelines for Participants (Appendix 1)
21 November 2022	- Clarified glycemic parameters and study discontinuation due to increased glycated hemoglobin (HbA1c) - Allowed adjustments to treatment medication at the discretion of the PI
26 January 2023	- Added plan for interim analysis

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported