Clinical trial results:
A Randomised, Double-Blind, Placebo-Controlled, Dose Finding Phase IIb Study to Assess the Efficacy and Safety of Orally Administered Epeleuton in Patients with Hypertriglyceridemia and Type 2 Diabetes.

Summary

EudraCT number	2020-000065-16
Trial protocol	DE LV
Global end of trial date	03 May 2022

Results information

Result version number	v1 (current)
This version publication date	26 May 2023
First version publication date	26 May 2023

Trial information

Trial identification

Sponsor protocol code	DS102A-07-CV1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04365400
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Afimmune
Sponsor organisation address	South County Business Park, Leopardstown, Dublin, Ireland, D18H5H9
Public contact	Regulatory Affairs Department, Afimmune, +353 12946380, afimmune.regulatory@afimmune.com
Scientific contact	Regulatory Affairs Department, Afimmune, +353 12946380, afimmune.regulatory@afimmune.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	19 October 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 May 2022
Global end of trial reached?	Yes
Global end of trial date	03 May 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Efficacy Objective:
• To assess the efficacy of orally administered Epeleuton capsules versus placebo, in the treatment of adult patients with hypertriglyceridemia and type 2 diabetes.

Safety Objective:
• To assess the safety of orally administered Epeleuton capsules versus placebo, in the treatment of adult patients with hypertriglyceridemia and type 2 diabetes.

Protection of trial subjects:

Investigators conducted the study according to the principles of the ICH E6 Guideline on GCP and the ethical principles that have their origins in the World Medical Association Declaration of Helsinki. The Investigator conducted all aspects of this study in accordance with all national, state and local laws or regulations.

Background therapy:

N/A

Evidence for comparator:

N/A

Actual start date of recruitment	03 August 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 26
Country: Number of subjects enrolled	Latvia: 24
Country: Number of subjects enrolled	Israel: 29
Country: Number of subjects enrolled	Georgia: 48
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Switzerland: 4
Country: Number of subjects enrolled	United States: 93
Worldwide total number of subjects	233
EEA total number of subjects	33

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)	153
From 65 to 84 years	80
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted in 7 countries.

Pre-assignment

Screening details:

In order to participate in this study, patients must meet all inclusion criteria and must not meet any of the exclusion criteria. Inclusion in the trial starts with the informed consent signature. The inclusion and exclusion criteria were verified at the first Screening Visit (Visit #1), confirmed at the second Screening Visit (Visit #2) and again

Period 1

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

Blinding implementation details:

All study site personnel, as well as the personnel involved in the monitoring or conduct of the study, were blinded to the individual patient treatment assignments. Randomisation details were kept strictly confidential, accessible only in an emergency to authorised persons, until the time of formal unblinding. The blinded code for the trial was broken only after all patient data had been recorded and verified and the database locked.

Arms

Are arms mutually exclusive?	Yes
Arm title	Epeleuton 2g

Arm description:

Two Epeleuton 500mg capsules and two placebo capsules orally administered twice a day, i.e. eight capsules daily for 26 weeks.

Arm type	Experimental
Investigational medicinal product name	Epeleuton 500mg Oral Capsules
Investigational medicinal product code	DS102
Other name	DS102 500mg Oral Capsules
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Two Epeleuton 500mg capsules and two placebo capsules orally administered twice a day, i.e. eight capsules daily for 26 weeks.

Arm title	Epeleuton 4g

Arm description:

Four Epeleuton 500mg capsules orally administered twice a day, i.e. eight capsules daily for 26 weeks.

Arm type	Experimental
Investigational medicinal product name	Epeleuton 500mg Oral Capsules
Investigational medicinal product code	DS102
Other name	DS102 500mg Oral Capsules
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Four Epeleuton 500mg capsules orally administered twice a day, i.e. eight capsules daily for 26 weeks.

Arm title	Placebo

Arm description:

Four placebo capsules orally administered twice a day, i.e. eight capsules daily for 26 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo 500mg Oral Capsules
Investigational medicinal product code	n/a
Other name	DS102 Placebo 500mg Oral Capsules
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Four placebo capsules orally administered twice a day, i.e. eight capsules daily for 26 weeks.

Number of subjects in period 1	Epeleuton 2g	Epeleuton 4g	Placebo
Started	79	77	77
Completed	49	50	50
Not completed	30	27	27
Consent withdrawn by subject	7	8	3
Physician decision	1	-	-
Related to early termination	18	13	-
Adverse event, non-fatal	3	5	6
Related to trial termination	-	-	17
Lost to follow-up	1	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Epeleuton 2g
Reporting group description:	
Two Epeleuton 500mg capsules and two placebo capsules orally administered twice a day, i.e. eight capsules daily for 26 weeks.	
Reporting group title	Epeleuton 4g
Reporting group description:	
Four Epeleuton 500mg capsules orally administered twice a day, i.e. eight capsules daily for 26 weeks.	
Reporting group title	Placebo
Reporting group description:	
Four placebo capsules orally administered twice a day, i.e. eight capsules daily for 26 weeks.	

Reporting group values	Epeleuton 2g	Epeleuton 4g	Placebo
Number of subjects	79	77	77
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	48	52	53
From 65-84 years	31	25	24
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	61.3	58.9	58.8
standard deviation	± 9.3	± 10.2	± 10.1
Gender categorical Units: Subjects			
Female	34	30	28
Male	45	47	49
Race/Ethnicity Units: Subjects			
White	75	74	70
Asian	1	2	4
Black or African American	2	1	1
Other	1	0	2

Reporting group values	Total		
Number of subjects	233		
Age categorical Units: Subjects			
In utero	0		

Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	153		
From 65-84 years	80		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	92		
Male	141		
Race/Ethnicity			
Units: Subjects			
White	219		
Asian	7		
Black or African American	4		
Other	3		

End points

End points reporting groups	
Reporting group title	Epeleuton 2g
Reporting group description:	
Two Epeleuton 500mg capsules and two placebo capsules orally administered twice a day, i.e. eight capsules daily for 26 weeks.	
Reporting group title	Epeleuton 4g
Reporting group description:	
Four Epeleuton 500mg capsules orally administered twice a day, i.e. eight capsules daily for 26 weeks.	
Reporting group title	Placebo
Reporting group description:	
Four placebo capsules orally administered twice a day, i.e. eight capsules daily for 26 weeks.	

Primary: Primary: Percent change in triglycerides from baseline to week 16.	
End point title	Primary: Percent change in triglycerides from baseline to week 16.
End point description:	
Percent change in triglycerides from baseline to week 16.	
End point type	Primary
End point timeframe:	
Up to 16 weeks	

End point values	Epeleuton 2g	Epeleuton 4g	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	74	76	
Units: % Change in TG				
arithmetic mean (standard error)	-7.886 (± 4.096)	5.273 (± 5.361)	-5.130 (± 4.945)	

Statistical analyses

Statistical analysis title	4g V Placebo
Comparison groups	Epeleuton 4g v Placebo
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.114812
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehmann Median
Point estimate	8.24

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.01
upper limit	18.19

Statistical analysis title	2g Vs Placebo
Comparison groups	Epeleuton 2g v Placebo
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.866847
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehmann Median
Point estimate	-0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.16
upper limit	7.96

Primary: Primary: Change in HbA1c from baseline to week 26.	
End point title	Primary: Change in HbA1c from baseline to week 26.
End point description: Change in HbA1c from baseline to week 26.	
End point type	Primary
End point timeframe: Up to 26 weeks	

End point values	Epeleuton 2g	Epeleuton 4g	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	74	76	
Units: % Change of HbA1C				
arithmetic mean (standard error)	-2.255 (± 1.412)	-0.524 (± 1.162)	-0.503 (± 1.446)	

Statistical analyses

Statistical analysis title	4g V Placebo
Comparison groups	Epeleuton 4g v Placebo

Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8658
Method	ANCOVA
Parameter estimate	Difference in change in HbA1c (%)
Point estimate	0.02516
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.26658
upper limit	0.316897

Statistical analysis title	2g Vs Placebo
Comparison groups	Epeleuton 2g v Placebo
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.65
Method	ANCOVA
Parameter estimate	Difference in change in HbA1c (%)
Point estimate	-0.07333
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.39012
upper limit	0.243455

Secondary: Secondary: Percent change in triglycerides from baseline to week 4

End point title	Secondary: Percent change in triglycerides from baseline to week 4
End point description:	
End point type	Secondary
End point timeframe:	
Up to 4 weeks	

End point values	Epeleuton 2g	Epeleuton 4g	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	74	76	
Units: % Change in TG				
arithmetic mean (standard error)	-9.301 (± 3.994)	5.965 (± 9.868)	-6.025 (± 4.479)	

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary: Percent change in triglycerides from baseline to week 8

End point title	Secondary: Percent change in triglycerides from baseline to week 8

End point description:

End point type	Secondary

End point timeframe:

Up to 8 weeks

End point values	Epeleuton 2g	Epeleuton 4g	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	74	76	
Units: % Change in TG				
arithmetic mean (standard error)	-5.018 (± 3.843)	-4.500 (± 4.623)	-5.242 (± 4.411)	

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary: Percent change in triglycerides from baseline to week 12

End point title	Secondary: Percent change in triglycerides from baseline to week 12

End point description:

End point type	Secondary

End point timeframe:

Up to 12 weeks

End point values	Epeleuton 2g	Epeleuton 4g	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	74	76	
Units: % Change in TG				
arithmetic mean (standard error)	-8.144 (± 4.071)	-4.215 (± 6.081)	4.022 (± 5.532)	

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary: Percent change in triglycerides from baseline to week 20

End point title	Secondary: Percent change in triglycerides from baseline to week 20

End point description:

End point type	Secondary

End point timeframe:

Up to 20 weeks

End point values	Epeleuton 2g	Epeleuton 4g	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	74	76	
Units: % Change in TG				
arithmetic mean (standard error)	-5.666 (± 4.665)	1.889 (± 5.005)	-4.270 (± 4.494)	

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary: Percent change in triglycerides from baseline to week 26

End point title	Secondary: Percent change in triglycerides from baseline to week 26

End point description:

End point type	Secondary

End point timeframe:

Up to 26 weeks

End point values	Epeleuton 2g	Epeleuton 4g	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	74	76	
Units: % Change in TG				
arithmetic mean (standard error)	-8.213 (± 4.882)	7.456 (± 6.585)	-0.675 (± 5.538)	

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary: Change in HbA1c from baseline to week 4

End point title	Secondary: Change in HbA1c from baseline to week 4

End point description:

End point type	Secondary

End point timeframe:

Up to 4 weeks

End point values	Epeleuton 2g	Epeleuton 4g	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	74	76	
Units: % Change in HbA1c				
arithmetic mean (standard error)	-2.606 (± 0.618)	-1.980 (± 0.683)	-1.365 (± 0.657)	

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary: Change in HbA1c from baseline to week 8

End point title	Secondary: Change in HbA1c from baseline to week 8

End point description:

End point type	Secondary

End point timeframe:

Up to 8 weeks

End point values	Epeleuton 2g	Epeleuton 4g	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	74	76	
Units: % Change in HbA1c				
arithmetic mean (standard error)	-3.327 (± 0.978)	-2.933 (± 0.815)	-2.913 (± 0.861)	

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary: Change in HbA1c from baseline to week 12

End point title	Secondary: Change in HbA1c from baseline to week 12

End point description:

End point type	Secondary

End point timeframe:

Up to 12 weeks

End point values	Epeleuton 2g	Epeleuton 4g	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	74	76	
Units: % Change in HbA1c				
arithmetic mean (standard error)	-3.448 (± 1.229)	-2.331 (± 1.052)	-1.315 (± 1.143)	

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary: Change in HbA1c from baseline to week 16

End point title	Secondary: Change in HbA1c from baseline to week 16

End point description:

End point type	Secondary

End point timeframe:

Up to 16 weeks

End point values	Epeleuton 2g	Epeleuton 4g	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	74	76	
Units: % Change in HbA1c				
arithmetic mean (standard error)	-2.690 (± 1.338)	-1.733 (± 1.110)	-1.278 (± 1.216)	

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary: Change in HbA1c from baseline to week 20

End point title	Secondary: Change in HbA1c from baseline to week 20

End point description:

End point type	Secondary

End point timeframe:

Up to 20 weeks

End point values	Epeleuton 2g	Epeleuton 4g	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	74	76	
Units: % Change in HbA1c				
arithmetic mean (standard error)	-4.176 (± 1.414)	-0.733 (± 1.188)	-0.811 (± 1.372)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 26 weeks

Adverse event reporting additional description:

An AE is defined as any untoward medical occurrence in a patient or clinical trial subject administered an IMP and which does not necessarily have a causal relationship with this treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Epeleuton 2g

Reporting group description:

Two Epeleuton 500mg capsules and two placebo capsules orally administered twice a day, i.e. eight capsules daily for 26 weeks.

Reporting group title	Epeleuton 4g

Reporting group description:

Four Epeleuton 500mg capsules orally administered twice a day, i.e. eight capsules daily for 26 weeks.

Reporting group title	Placebo

Reporting group description:

Four placebo capsules orally administered twice a day, i.e. eight capsules daily for 26 weeks.

Serious adverse events	Epeleuton 2g	Epeleuton 4g	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	1 / 77 (1.30%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Acute Myocardial Infarction			
subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (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

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

Non-serious adverse events	Epeleuton 2g	Epeleuton 4g	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 79 (62.03%)	52 / 77 (67.53%)	42 / 77 (54.55%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous Cell Carcinoma of Skin			
subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 79 (6.33%)	0 / 77 (0.00%)	3 / 77 (3.90%)
occurrences (all)	5	0	3
Labile Hypertension			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 79 (2.53%)	0 / 77 (0.00%)	2 / 77 (2.60%)
occurrences (all)	2	0	2
Fatigue			
subjects affected / exposed	1 / 79 (1.27%)	2 / 77 (2.60%)	1 / 77 (1.30%)
occurrences (all)	2	2	1
Chest Pain			
subjects affected / exposed	2 / 79 (2.53%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	2	0	0
Oedema Peripheral			
subjects affected / exposed	2 / 79 (2.53%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	2	0	0
Pyrexia			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	2	0	2
Hunger			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Malaise			

subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Vaccination Site Pain			
subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Immune system disorders			
Immunisation Reaction			
subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	2 / 77 (2.60%)
occurrences (all)	0	0	2
Drug Hypersensitivity			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Seasonal Allergy			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Prostatic Dysplasia			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Vaginal Haemorrhage			
subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	2 / 77 (2.60%)
occurrences (all)	0	0	2
Oropharyngeal Pain			
subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	2 / 77 (2.60%)
occurrences (all)	0	0	2
Asthma			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			

subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Increased Upper Airway Secretion			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 79 (1.27%)	1 / 77 (1.30%)	1 / 77 (1.30%)
occurrences (all)	1	1	1
Depression			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	2 / 77 (2.60%)
occurrences (all)	0	1	2
Blood Triglycerides Increased			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	1	0	1
Glomerular Filtration Rate Decreased			
subjects affected / exposed	0 / 79 (0.00%)	2 / 77 (2.60%)	0 / 77 (0.00%)
occurrences (all)	0	2	0
Albumin Urine Present			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Blood Cholesterol Increased			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Blood Glucose Increased			
subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Blood Insulin Increased			
subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Blood Pressure Increased			

subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Body Temperature Increased			
subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Electrocardiogram QRS Complex Abnormal			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Electrocardiogram T Wave Abnormal			
subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Glycosylated Haemoglobin Increased			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	2	0
International Normalised Ratio Increased			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Intraocular Pressure Increased			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Mean Cell Haemoglobin Concentration Decreased			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Mean Cell Haemoglobin Decreased			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Mean Cell Volume Decrease			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Occult Blood Positive			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
QRS Axis Abnormal			

subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
SARS-CoV-2 Test Positive			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Burns Third Degree			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Conjunctival Abrasion			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Fall			
subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Post Procedural Complication			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Atrioventricular Block First Degree			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	1 / 77 (1.30%)
occurrences (all)	0	1	1
Defect Conduction Intraventricular			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	1	0	1
Bundle Branch Block Left			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Bundle Branch Block Right			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Cardiac Failure			

subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Myocardial Infarction			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Sinus Tachycardia			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 79 (3.80%)	1 / 77 (1.30%)	2 / 77 (2.60%)
occurrences (all)	3	1	2
Dysgeusia			
subjects affected / exposed	1 / 79 (1.27%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	1	1	0
Taste Disorder			
subjects affected / exposed	1 / 79 (1.27%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	1	1	0
Carotid Artery Stenosis			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	2	0
Carpal Tunnel Syndrome			
subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Depressed level of Consciousness			
subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Hypoaesthesia			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Lacunar Stroke			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Migraine			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0

Sciatica			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Vocal Cord Paralysis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 79 (1.27%)	2 / 77 (2.60%)	0 / 77 (0.00%)
occurrences (all)	1	2	0
Lymphadenopathy			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 79 (0.00%)	3 / 77 (3.90%)	0 / 77 (0.00%)
occurrences (all)	0	3	0
Ear Pain			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Open Angle Glaucoma			
subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Vitreous Detachment			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	8 / 79 (10.13%)	13 / 77 (16.88%)	6 / 77 (7.79%)
occurrences (all)	10	17	6
Nausea			
subjects affected / exposed	2 / 79 (2.53%)	6 / 77 (7.79%)	3 / 77 (3.90%)
occurrences (all)	2	6	4

Dyspepsia			
subjects affected / exposed	3 / 79 (3.80%)	2 / 77 (2.60%)	2 / 77 (2.60%)
occurrences (all)	4	2	3
Abdominal Pain			
subjects affected / exposed	1 / 79 (1.27%)	3 / 77 (3.90%)	1 / 77 (1.30%)
occurrences (all)	3	4	1
Eructation			
subjects affected / exposed	2 / 79 (2.53%)	3 / 77 (3.90%)	0 / 77 (0.00%)
occurrences (all)	2	3	0
Flatulence			
subjects affected / exposed	0 / 79 (0.00%)	3 / 77 (3.90%)	1 / 77 (1.30%)
occurrences (all)	0	3	1
Gastroesophageal reflux disease			
subjects affected / exposed	2 / 79 (2.53%)	2 / 77 (2.60%)	0 / 77 (0.00%)
occurrences (all)	2	3	0
Abdominal Distension			
subjects affected / exposed	1 / 79 (1.27%)	1 / 77 (1.30%)	1 / 77 (1.30%)
occurrences (all)	1	1	1
Constipation			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	2 / 77 (2.60%)
occurrences (all)	1	0	2
Vomiting			
subjects affected / exposed	2 / 79 (2.53%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	2	1	0
Abdominal Pain Upper			
subjects affected / exposed	2 / 79 (2.53%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	2	0	0
Abdominal Discomfort			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Dental Caries			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	2	0	0
Diverticulum			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0

Dry Mouth			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Frequent Bowel Movements			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Gastritis			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal Pain			
subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	2	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 79 (1.27%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	1	1	0
Diabetic Foot			
subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Macule			
subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	2	0
Urticaria			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Albuminuria			
subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Glycosuria			

subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Haematuria			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Microalbuminuria			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Pollakiuria			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Proteinuria			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Renal Impairment			
subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 79 (1.27%)	1 / 77 (1.30%)	1 / 77 (1.30%)
occurrences (all)	1	1	1
Back Pain			
subjects affected / exposed	1 / 79 (1.27%)	2 / 77 (2.60%)	0 / 77 (0.00%)
occurrences (all)	1	2	0
Myalgia			
subjects affected / exposed	2 / 79 (2.53%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	2	1	0
Exostosis			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	1	0	1
Muscle Spasms			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	1	0	1
Arthritis			

subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Fibromyalgia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Intervertebral Disc Protrusion			
subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Osteoarthritis			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Pain In Extremity			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Synovial Cyst			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	7 / 79 (8.86%)	2 / 77 (2.60%)	5 / 77 (6.49%)
occurrences (all)	8	3	7
Lower Respiratory Tract Infection			
subjects affected / exposed	1 / 79 (1.27%)	1 / 77 (1.30%)	2 / 77 (2.60%)
occurrences (all)	1	1	2
Nasopharyngitis			
subjects affected / exposed	0 / 79 (0.00%)	2 / 77 (2.60%)	1 / 77 (1.30%)
occurrences (all)	0	2	1
Respiratory Tract Infection			
subjects affected / exposed	1 / 79 (1.27%)	2 / 77 (2.60%)	0 / 77 (0.00%)
occurrences (all)	1	2	0
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 79 (1.27%)	2 / 77 (2.60%)	0 / 77 (0.00%)
occurrences (all)	1	2	0
Conjunctivitis			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	1	0	1

Urinary Tract Infection			
subjects affected / exposed	2 / 79 (2.53%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	2	0	0
Asymptomatic COVID-19			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Cystitis			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Diarrhoea Infectious			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Fungal Infection			
subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Giardiasis			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Pharyngitis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Pulpitis Dental			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Vulvovaginal Candidiasis			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0

Metabolism and nutrition disorders			
Type 2 Diabetes Mellitus			
subjects affected / exposed	4 / 79 (5.06%)	1 / 77 (1.30%)	1 / 77 (1.30%)
occurrences (all)	4	1	1
Hyperglycaemia			
subjects affected / exposed	4 / 79 (5.06%)	1 / 77 (1.30%)	1 / 77 (1.30%)
occurrences (all)	4	1	1
Hypertriglyceridemia			
subjects affected / exposed	0 / 79 (0.00%)	4 / 77 (5.19%)	0 / 77 (0.00%)
occurrences (all)	0	4	0
Diabetes Mellitus			
subjects affected / exposed	1 / 79 (1.27%)	0 / 77 (0.00%)	2 / 77 (2.60%)
occurrences (all)	1	0	2
Decreased Appetite			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Hypoglycaemia			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	1
Iron Deficiency			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Joint Swelling			
subjects affected / exposed	0 / 79 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 January 2021	• Administrative Updates • Changes made to synopsis and text in point 2 of inclusion criteria section • Changes made to synopsis and text in point 3 of inclusion criteria section • Changes made to synopsis and text in point 8 of inclusion criteria section and point 13 of exclusion criteria section • Changes made to synopsis and text in point 9 of inclusion criteria section, deletion of point 1 of exclusion criteria section and addition of point 25 of exclusion criteria • Changes made throughout the protocol to add pregnancy testing and contraceptive counselling • Changes made to synopsis and text in point 9 of exclusion criteria section • Changes made to synopsis and text in point 27 of exclusion criteria section • Changes made throughout where diary is mentioned • Changes made to vital sign section • Addition of Interim Analysis Section • Addition of COVID-19 Contingency Section
14 June 2021	• Administrative Updates • Change made to LDL inclusion • Change made to BMI inclusion • Change to allow basal insulin • Addition of inclusion/exclusion criteria review at screening 2 • Addition of urine pregnancy test at baseline • Clarification that pre-trial background medication should stay stable through the study • Changes made to adverse event reporting • Changes made to unblinding procedure
14 February 2022	• Administrative Updates • Change to Statistical Methodology Section • Update to Interim Analysis Section • Clarification made to Exclusion 28. • Clarification on Protocol Deviations

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None reported

Notes: