Clinical trial results:
A Double-Blind, Placebo-Controlled, Cross-over Phase II Study to Evaluate the Effect of a 6-week Elafibranor (120mg) treatment administered once daily on hepatic lipid composition in subjects with Nonalcoholic Fatty Liver (NAFL).

Summary

EudraCT number	2019-000645-12
Trial protocol	NL
Global end of trial date	14 July 2020

Results information

Result version number	v1 (current)
This version publication date	24 November 2021
First version publication date	24 November 2021

Trial information

Trial identification

Sponsor protocol code	GFT505-219-8

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03953456
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GENFIT
Sponsor organisation address	Parc Eurasanté, 885, Avenue Eugène Avinée, Loos, France, 59120
Public contact	clinicaltrial@genfit.com , GENFIT, +33 320164038,
Scientific contact	Carol Addy, MD MMSc, GENFIT, +01 6179536469,

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	14 July 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 July 2020
Global end of trial reached?	Yes
Global end of trial date	14 July 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to evaluate the effect of a 6-week treatment with elafibranor versus placebo on hepatic lipid composition in subjects with a fatty liver.
The secondary objectives were to evaluate the between-treatment difference (elafibranor 120 mg/day vs. placebo) in hepatic glucose production (HGP) measured at the end of 6 weeks of treatment, and to compare the changes from baseline achieved after 6 weeks of treatment with elafibranor 120 mg/day versus placebo in glucose homeostasis, lipid metabolism, inflammatory markers, liver function, renal function and anthropometry.
The safety objectives were to assess the safety and tolerability profile of 6 weeks elafibranor administration orally (120 mg/day) in NAFL subjects in terms of serious adverse events (SAE), adverse events (AE), vital signs, haematological parameters, liver markers, renal biomarkers, metabolic parameters and other biochemical safety markers.

Protection of trial subjects:

This study was conducted in accordance with Good Clinical Practice standards, ethical principles stated in the Declaration of Helsinki and applicable regulatory requirements. After the subject has ended his/her participation in the trial, the investigator provided appropriate medication and/or arranged access to appropriate care for the patient.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 August 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 17
Worldwide total number of subjects	17
EEA total number of subjects	17

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)	5
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A liver fat percentage (intrahepatic lipid [IHL]) of ≥5% as determined with magnetic resonance spectroscopy (1H-MRS), body mass index (BMI) between 25 and 38 kg/m2, and age between 40 and 75 years.

Pre-assignment

Screening details:

A total of 36 subjects were screened for the study: 19 subjects were screen failures (18 subjects did not meet the study eligibility criteria and 1 subject had low quality 1H-MRS data that made determination of liver fat composition not possible) and 17 subjects were eligible and randomised.

Period 1

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

Blinding implementation details:

A randomisation list was generated by a random number system. Individual randomisation code referred to either of the two sequence groups: sequence Group A: placebo first followed by elafibranor 120mg, sequence Group B: elafibranor 120mg first followed by placebo. The subjects who successfully passed screening were assigned an individual randomisation code and randomly allocated to one of the two sequence groups (A or B).

Arms

Are arms mutually exclusive?	No
Arm title	Elafibranor 120 mg

Arm description:

Elafibranor 120 mg tablet qd

Arm type	Experimental
Investigational medicinal product name	Elafibranor
Investigational medicinal product code	GFT505
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Elafibranor 120 mg was administered orally to study subjects once daily for 6 weeks.

Arm title	Placebo

Arm description:

Matched placebo tablet qd

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

Dosage and administration details:

Placebo was administered orally to study subjects once daily for 6 weeks.

Number of subjects in period 1	Elafibranor 120 mg	Placebo
Started	13	13
Completed	12	11
Not completed	1	2
Study interrupted due to COVID-19 pandemic	1	2

Baseline characteristics

Reporting groups	
Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	17	17	
Age categorical			
To be eligible to participate in this study, a subject had to be male or a post-menopausal female aged 40 to 75 years, inclusive, at the first Screening Visit. Post-menopausal was defined as surgically sterilised at least 6 months previously or having had no spontaneous menses for at least 1 year prior to screening.			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	5	5	
From 65-84 years	12	12	
85 years and over	0	0	
Adults until 64 years	0	0	
Adults up to 64 years inclusive	0	0	
Adults aged 65 to 74 years inclusive	0	0	
51 to 64 years inclusive	0	0	
Age continuous			
Units: years			
arithmetic mean	65.6		
standard deviation	± 8.2	-	
Gender categorical			
Units: Subjects			
Female	3	3	
Male	14	14	
Alcohol consumption			
Subjects were excluded from the study if they presented a current or recent history (<5 years) of significant alcohol consumption. For men, significant consumption was typically defined as more than 30 g pure alcohol per day; for women, it was typically defined as more than 20 g pure alcohol per day.			
Units: Subjects			
No alcohol consumption	3	3	
Current alcohol consumption	14	14	
Smoking status			
Smoking was an exclusion criterion.			
Units: Subjects			
Current smoker	0	0	
Not a current smoker	17	17	
Dietary habits and lifestyle			
Is the patient currently following a diet or strenuous physical activity to lose weight			

Units: Subjects			
Current practice to lose weight	0	0	
No attempted practice to lose weight	17	17	
Race Units: Subjects			
American Indian or Alaska Native	0	0	
Native Hawaiian or other Pacific Islander	0	0	
Asian	0	0	
White	17	17	
Black or African American	0	0	
Other	0	0	
BMI categorical Units: Subjects			
<18.5 kg/m2	0	0	
[18.5 - 25 [kg/m2	0	0	
[25 - 30 [kg/m2	9	9	
30 =<	8	8	
BMI			
Subjects had to present a BMI of ≥25.0 kg/m2 but ≤38.0 kg/m2 to be included in the study			
Units: kg/m2			
arithmetic mean	30.5		
standard deviation	± 2.3	-	
Waist circumference			
Waist circumference was measured at the midpoint between the lateral iliac crest and lowest rib, during expiration. The measuring tape was to be snug but not compressing the skin and held parallel to the floor. The measurement was to be made during normal respiration.			
Units: cm			
arithmetic mean	110.2		
standard deviation	± 7.3	-	
Fat mass (absolute)			
The Bod Pod® (Cosmed) was used to determine body composition and measure fat mass, fat-free mass, and total body mass via whole body densitometry. Measurements were made with the subject sitting inside a comfortable chamber for two 50-second measurements; the total duration of the procedure was approximately 5 minutes.			
Units: kg			
arithmetic mean	35.51		
standard deviation	± 8.58	-	
Fat mass (relative)			
The Bod Pod® (Cosmed) was used to determine body composition and measure fat mass, fat-free mass, and total body mass via whole body densitometry. Measurements were made with the subject sitting inside a comfortable chamber, for two 50-second measurements; the total duration of the procedure was approximately 5 minutes.			
Units: percentage			
arithmetic mean	38.35		
standard deviation	± 7.57	-	
Fat free mass (absolute)			
The Bod Pod® (Cosmed) was used to determine body composition and measure fat mass, fat-free mass, and total body mass via whole body densitometry. Measurements were made with the subject sitting inside a comfortable chamber, for two 50-second measurements; the total duration of the procedure was approximately 5 minutes.			
Units: kg			
arithmetic mean	56.70		
standard deviation	± 7.79	-	

Fat free mass (relative)			
The Bod Pod® (Cosmed) was used to determine body composition and measure fat mass, fat-free mass, and total body mass via whole body densitometry. Measurements were made with the subject sitting inside a comfortable chamber, for two 50-second measurements; the total duration of the procedure was approximately 5 minutes.			
Units: percentage			
arithmetic mean	61.65		
standard deviation	± 7.57	-	
Body mass			
The Bod Pod® (Cosmed) was used to determine body composition and measure fat mass, fat-free mass, and total body mass via whole body densitometry. Measurements were made with the subject sitting inside a comfortable chamber, for two 50-second measurements; the total duration of the procedure was approximately 5 minutes.			
Units: kg			
arithmetic mean	92.20		
standard deviation	± 9.30	-	

Subject analysis sets

Subject analysis set title	ITT set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All the subjects that were randomized.	
Subject analysis set title	PP set
Subject analysis set type	Per protocol
Subject analysis set description:	
All randomized subjects who completed the study without any major protocol deviation affecting the primary efficacy endpoint.	
Subject analysis set title	Safety set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects who received at least one dose of study treatment.	

Reporting group values	ITT set	PP set	Safety set
Number of subjects	17	6	17
Age categorical			
To be eligible to participate in this study, a subject had to be male or a post-menopausal female aged 40 to 75 years, inclusive, at the first Screening Visit. Post-menopausal was defined as surgically sterilised at least 6 months previously or having had no spontaneous menses for at least 1 year prior to screening.			
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)	5	3	5
From 65-84 years	12	3	12
85 years and over	0	0	0
Adults until 64 years	0	0	0
Adults up to 64 years inclusive	0	0	0
Adults aged 65 to 74 years inclusive	0	0	0

51 to 64 years inclusive	0	0	0

Age continuous			
Units: years			
arithmetic mean	65.6	-	65.6
standard deviation	± 8.2	±	± 8.2
Gender categorical			
Units: Subjects			
Female	3		3
Male	14		14
Alcohol consumption			
Subjects were excluded from the study if they presented a current or recent history (<5 years) of significant alcohol consumption. For men, significant consumption was typically defined as more than 30 g pure alcohol per day; for women, it was typically defined as more than 20 g pure alcohol per day.			
Units: Subjects			
No alcohol consumption	3		3
Current alcohol consumption	14		14
Smoking status			
Smoking was an exclusion criterion.			
Units: Subjects			
Current smoker	0		0
Not a current smoker	17		17
Dietary habits and lifestyle			
Is the patient currently following a diet or strenuous physical activity to lose weight			
Units: Subjects			
Current practice to lose weight	0		0
No attempted practice to lose weight	17		17
Race			
Units: Subjects			
American Indian or Alaska Native	0		0
Native Hawaiian or other Pacific Islander	0		0
Asian	0		0
White	17		17
Black or African American	0		0
Other	0		0
BMI categorical			
Units: Subjects			
<18.5 kg/m2	0		0
[18.5 - 25 [kg/m2	0		0
[25 - 30 [kg/m2	9		9
30 =<	8		8
BMI			
Subjects had to present a BMI of ≥25.0 kg/m2 but ≤38.0 kg/m2 to be included in the study			
Units: kg/m2			
arithmetic mean	30.5		30.5
standard deviation	± 2.3	±	± 2.3
Waist circumference			
Waist circumference was measured at the midpoint between the lateral iliac crest and lowest rib, during expiration. The measuring tape was to be snug but not compressing the skin and held parallel to the floor. The measurement was to be made during normal respiration.			

Units: cm			
arithmetic mean	110.2		110.2
standard deviation	± 7.3	±	± 7.3
Fat mass (absolute)			
The Bod Pod® (Cosmed) was used to determine body composition and measure fat mass, fat-free mass, and total body mass via whole body densitometry. Measurements were made with the subject sitting inside a comfortable chamber for two 50-second measurements; the total duration of the procedure was approximately 5 minutes.			
Units: kg			
arithmetic mean	35.51		35.51
standard deviation	± 8.58	±	± 8.58
Fat mass (relative)			
The Bod Pod® (Cosmed) was used to determine body composition and measure fat mass, fat-free mass, and total body mass via whole body densitometry. Measurements were made with the subject sitting inside a comfortable chamber, for two 50-second measurements; the total duration of the procedure was approximately 5 minutes.			
Units: percentage			
arithmetic mean	38.35		38.35
standard deviation	± 7.57	±	± 7.57
Fat free mass (absolute)			
The Bod Pod® (Cosmed) was used to determine body composition and measure fat mass, fat-free mass, and total body mass via whole body densitometry. Measurements were made with the subject sitting inside a comfortable chamber, for two 50-second measurements; the total duration of the procedure was approximately 5 minutes.			
Units: kg			
arithmetic mean	56.70		56.70
standard deviation	± 7.79	±	± 7.79
Fat free mass (relative)			
The Bod Pod® (Cosmed) was used to determine body composition and measure fat mass, fat-free mass, and total body mass via whole body densitometry. Measurements were made with the subject sitting inside a comfortable chamber, for two 50-second measurements; the total duration of the procedure was approximately 5 minutes.			
Units: percentage			
arithmetic mean	61.65		61.65
standard deviation	± 7.57	±	± 7.57
Body mass			
The Bod Pod® (Cosmed) was used to determine body composition and measure fat mass, fat-free mass, and total body mass via whole body densitometry. Measurements were made with the subject sitting inside a comfortable chamber, for two 50-second measurements; the total duration of the procedure was approximately 5 minutes.			
Units: kg			
arithmetic mean	92.20		92.20
standard deviation	± 9.30	±	± 9.30

End points

End points reporting groups

Reporting group title	Elafibranor 120 mg
Reporting group description: Elafibranor 120 mg tablet qd	
Reporting group title	Placebo
Reporting group description: Matched placebo tablet qd	
Subject analysis set title	ITT set
Subject analysis set type	Intention-to-treat
Subject analysis set description: All the subjects that were randomized.	
Subject analysis set title	PP set
Subject analysis set type	Per protocol
Subject analysis set description: All randomized subjects who completed the study without any major protocol deviation affecting the primary efficacy endpoint.	
Subject analysis set title	Safety set
Subject analysis set type	Safety analysis
Subject analysis set description: All subjects who received at least one dose of study treatment.	

Primary: relative amount of saturated fatty acid in the liver (%SFA) at the end of each 6-week treatment period

End point title	relative amount of saturated fatty acid in the liver (%SFA) at the end of each 6-week treatment period[1]
End point description: The primary endpoint was the relative amount of SFA in the liver (%SFA) measured by 1H-MRS at the end of each 6-week treatment period.	
End point type	Primary
End point timeframe: Visit 3 and Visit 6	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No efficacy analyses produced as the number of subjects who completed the study was insufficient.

End point values	Elafibranor 120 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: percentage				
arithmetic mean (standard deviation)	()	()		

Notes:

[2] - analysis not performed due to lack of data

[3] - analysis not performed due to lack of data

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline achieved after 6 weeks of treatment in Polyunsaturated Fatty Acids (PUFA)

End point title	Change from baseline achieved after 6 weeks of treatment in Polyunsaturated Fatty Acids (PUFA)[4]

End point description:

Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Primary

End point timeframe:

Visit 3 and Visit 6

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No efficacy analyses produced as the number of subjects who completed the study was insufficient.

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[5]	0[6]	0[7]	0[8]
Units: percentage				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[5] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[6] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[7] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[8] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline achieved after 6 weeks of treatment in Monounsaturated Fatty Acids (MUFA)

End point title	Change from baseline achieved after 6 weeks of treatment in Monounsaturated Fatty Acids (MUFA)[9]

End point description:

Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Primary

End point timeframe:

Visit 3 and Visit 6

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No efficacy analyses produced as the number of subjects who completed the study was insufficient.

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[10]	0[11]	0[12]	0[13]
Units: percentage				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[10] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[11] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[12] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[13] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline achieved after 6 weeks of treatment in Saturated Fatty Acids (SFA)

End point title	Change from baseline achieved after 6 weeks of treatment in Saturated Fatty Acids (SFA)[14]

End point description:

Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Primary

End point timeframe:

Visit 3 and Visit 6

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No efficacy analyses produced as the number of subjects who completed the study was insufficient.

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[15]	0[16]	0[17]	0[18]
Units: percentage				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[15] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[16] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[17] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[18] - No efficacy analyses produced as the number of subjects who completed the study was

insufficient.

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline achieved after 6 weeks of treatment in MRS liver fat fraction (%Fat w/w)

End point title	Change from baseline achieved after 6 weeks of treatment in MRS liver fat fraction (%Fat w/w)[19]

End point description:

Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Primary

End point timeframe:

Visit 3 and Visit 6

Notes:

[19] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No efficacy analyses produced as the number of subjects who completed the study was insufficient.

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[20]	0[21]	0[22]	0[23]
Units: percentage				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[20] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[21] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[22] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[23] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Hepatic Glucose Production (HGP) at the end of each 6-week treatment period

End point title	Hepatic Glucose Production (HGP) at the end of each 6-week treatment period

End point description:

Hepatic glucose production at the end of each 6-week treatment period was used as a measure of hepatic insulin sensitivity.

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[24]	0[25]	0[26]	0[27]
Units: µmol/kg/min				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[24] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[25] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[26] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[27] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in HbA1c

End point title	Change from baseline achieved after 6 weeks of treatment in HbA1c

End point description:

Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[28]	0[29]	0[30]	0[31]
Units: percentage				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[28] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[29] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[30] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[31] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in fasting plasma glucose (FPG)

End point title	Change from baseline achieved after 6 weeks of treatment in fasting plasma glucose (FPG)

End point description:

Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[32]	0[33]	0[34]	0[35]
Units: mmol/L				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[32] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[33] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[34] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[35] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in fasting insulin

End point title	Change from baseline achieved after 6 weeks of treatment in

	fasting insulin

End point description:

Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[36]	0[37]	0[38]	0[39]
Units: pmol/L				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[36] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[37] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[38] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[39] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in HOMA-IR

End point title	Change from baseline achieved after 6 weeks of treatment in HOMA-IR

End point description:

HOMA-IR: homeostasis model assessment of insulin resistance
Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[40]	0[41]	0[42]	0[43]
Units: index				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[40] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[41] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[42] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[43] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in fructosamine

End point title	Change from baseline achieved after 6 weeks of treatment in fructosamine

End point description:

Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[44]	0[45]	0[46]	0[47]
Units: µmol/L				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[44] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[45] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[46] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[47] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in C-peptide

End point title	Change from baseline achieved after 6 weeks of treatment in C-peptide

End point description:

Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[48]	0[49]	0[50]	0[51]
Units: nmol/L				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[48] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[49] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[50] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[51] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in total cholesterol

End point title	Change from baseline achieved after 6 weeks of treatment in total cholesterol

End point description:

Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[52]	0[53]	0[54]	0[55]
Units: mmol/L				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[52] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[53] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[54] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[55] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in HDL cholesterol (HDL-C)

End point title	Change from baseline achieved after 6 weeks of treatment in HDL cholesterol (HDL-C)

End point description:

HDL: high density lioprotein
Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[56]	0[57]	0[58]	0[59]
Units: mmol/L				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[56] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[57] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[58] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[59] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in non-HDL cholesterol

End point title	Change from baseline achieved after 6 weeks of treatment in non-HDL cholesterol

End point description:

Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[60]	0[61]	0[62]	0[63]
Units: mmol/L				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[60] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[61] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[62] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[63] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in LDL cholesterol (calculated)

End point title	Change from baseline achieved after 6 weeks of treatment in LDL cholesterol (calculated)

End point description:

LDL: low density lipoprotein
Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[64]	0[65]	0[66]	0[67]
Units: mmol/L				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[64] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[65] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[66] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[67] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in fasting triglycerides

End point title	Change from baseline achieved after 6 weeks of treatment in fasting triglycerides

End point description:

Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[68]	0[69]	0[70]	0[71]
Units: mmol/L				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[68] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[69] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[70] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[71] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in free fatty acid

End point title	Change from baseline achieved after 6 weeks of treatment in free fatty acid

End point description:

Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[72]	0[73]	0[74]	0[75]
Units: mmol/L				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[72] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[73] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[74] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[75] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in high-sensitivity C-reactive protein hsCRP

End point title	Change from baseline achieved after 6 weeks of treatment in high-sensitivity C-reactive protein hsCRP

End point description:

hs-CRP: high sensitivity C-reactive protein
Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[76]	0[77]	0[78]	0[79]
Units: mg/L				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[76] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[77] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[78] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[79] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in fibrinogen

End point title	Change from baseline achieved after 6 weeks of treatment in fibrinogen

End point description:

Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[80]	0[81]	0[82]	0[83]
Units: µmol/L				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[80] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[81] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[82] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[83] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in haptoglobin

End point title	Change from baseline achieved after 6 weeks of treatment in haptoglobin

End point description:

Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[84]	0[85]	0[86]	0[87]
Units: g/L				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[84] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[85] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[86] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[87] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in gamma-glutamyl transferase (GGT)

End point title	Change from baseline achieved after 6 weeks of treatment in gamma-glutamyl transferase (GGT)

End point description:

Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[88]	0[89]	0[90]	0[91]
Units: IU/L				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[88] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[89] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[90] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[91] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in aspartate aminotransferase (AST)

End point title	Change from baseline achieved after 6 weeks of treatment in aspartate aminotransferase (AST)

End point description:

Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[92]	0[93]	0[94]	0[95]
Units: IU/L				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[92] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[93] - No efficacy analyses produced as the number of subjects who completed the study was

insufficient.

[94] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[95] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in alanine aminotransferase (ALT)

End point title	Change from baseline achieved after 6 weeks of treatment in alanine aminotransferase (ALT)

End point description:

Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[96]	0[97]	0[98]	0[99]
Units: IU/L				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[96] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[97] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[98] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[99] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in alkaline phosphatase

End point title	Change from baseline achieved after 6 weeks of treatment in alkaline phosphatase

End point description:

Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[100]	0[101]	0[102]	0[103]
Units: IU/L				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[100] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[101] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[102] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[103] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in total bilirubin

End point title	Change from baseline achieved after 6 weeks of treatment in total bilirubin

End point description:

Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[104]	0[105]	0[106]	0[107]
Units: µmol/L				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[104] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[105] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[106] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[107] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in conjugated bilirubin

End point title	Change from baseline achieved after 6 weeks of treatment in conjugated bilirubin

End point description:

Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[108]	0[109]	0[110]	0[111]
Units: µmol/L				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[108] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[109] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[110] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[111] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in serum creatinine

End point title	Change from baseline achieved after 6 weeks of treatment in serum creatinine

End point description:

Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[112]	0[113]	0[114]	0[115]
Units: µmol/L				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[112] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[113] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[114] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[115] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in eGFR

End point title	Change from baseline achieved after 6 weeks of treatment in eGFR

End point description:

eGFR, i.e. estimated glomerular filtration rate, was calculated according to the MDRD (Modification of Diet in Renal Disease) equation.
Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[116]	0[117]	0[118]	0[119]
Units: mL/min/1.73m2				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[116] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[117] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[118] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[119] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in albumin

End point title	Change from baseline achieved after 6 weeks of treatment in albumin

End point description:

Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[120]	0[121]	0[122]	0[123]
Units: g/L				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[120] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[121] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[122] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[123] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in total protein

End point title	Change from baseline achieved after 6 weeks of treatment in total protein

End point description:

Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[124]	0[125]	0[126]	0[127]
Units: g/L				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[124] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[125] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[126] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[127] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in urea (BUN)

End point title	Change from baseline achieved after 6 weeks of treatment in urea (BUN)

End point description:

Urea: blood urea nitrogen
Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[128]	0[129]	0[130]	0[131]
Units: mmol/L				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[128] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[129] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[130] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[131] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in uric acid

End point title	Change from baseline achieved after 6 weeks of treatment in uric acid

End point description:

Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[132]	0[133]	0[134]	0[135]
Units: µmol/L				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[132] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[133] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[134] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[135] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in body weight

End point title	Change from baseline achieved after 6 weeks of treatment in body weight

End point description:

Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[136]	0[137]	0[138]	0[139]
Units: kg				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[136] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[137] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[138] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[139] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline achieved after 6 weeks of treatment in Body Mass Index (BMI)

End point title	Change from baseline achieved after 6 weeks of treatment in Body Mass Index (BMI)

End point description:

Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[140]	0[141]	0[142]	0[143]
Units: kg/m2				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[140] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[141] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[142] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[143] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: Waist circumference Change from baseline at the end of each 6-week treatment period

End point title	Waist circumference Change from baseline at the end of each 6-week treatment period

End point description:

Secondary endpoints were measured at the end of each of the 6-week treatment periods

End point type	Secondary

End point timeframe:

Visit 3 and Visit 6

End point values	Elafibranor 120 mg	Placebo	ITT set	PP set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[144]	0[145]	0[146]	0[147]
Units: cm				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[144] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[145] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[146] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

[147] - No efficacy analyses produced as the number of subjects who completed the study was insufficient.

Statistical analyses

No statistical analyses for this end point

Secondary: incidence of clinically significant hematology parameter abnormality

End point title	incidence of clinically significant hematology parameter abnormality

End point description:

abnormalities considered clinically significant by the PI.

End point type	Secondary

End point timeframe:

from the first screening visit until Visit 6 of the second treatment period

End point values	Elafibranor 120 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: number of subjects with abnormalities	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: incidence of clinically significant chemistry, liver function and renal function parameter abnormality

End point title	incidence of clinically significant chemistry, liver function and renal function parameter abnormality

End point description:

abnormalities considered clinically significant by the PI

End point type	Secondary

End point timeframe:

from the first screening visit until Visit 6 of the second treatment period

End point values	Elafibranor 120 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: number of subjects with abnormalities	2	2		

Statistical analyses

No statistical analyses for this end point

Secondary: incidence of clinically significant vital signs abnormality

End point title	incidence of clinically significant vital signs abnormality

End point description:

abnormalities considered clinically significant by the PI

End point type	Secondary

End point timeframe:

from the first screening visit until Visit 6 of the second treatment period

End point values	Elafibranor 120 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: number of subjects with abnormalities	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: incidence of clinically significant change in diet

End point title	incidence of clinically significant change in diet

End point description:

changes considered clinically significant by the PI

End point type	Secondary

End point timeframe:

from the first screening visit until Visit 6 of the second treatment period

End point values	Elafibranor 120 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: number of subjects with CS change	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: incidence of clinically significant change in alcohol consumption

End point title	incidence of clinically significant change in alcohol consumption

End point description:

changes considered clinically significant by the PI

End point type	Secondary

End point timeframe:

from the first screening visit until Visit 6 of the second treatment period

End point values	Elafibranor 120 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: number of subjects with CS change	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: incidence of clinically significant change in physical activity

End point title	incidence of clinically significant change in physical activity

End point description:

changes considered clinically significant by the PI

End point type	Secondary

End point timeframe:

from the first screening visit until Visit 6 of the second treatment period

End point values	Elafibranor 120 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: number of subjects with CS change	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: incidence of strenuous and unusual exercise

End point title	incidence of strenuous and unusual exercise

End point description:

End point type	Secondary

End point timeframe:

from the first screening visit until Visit 6 of the second treatment period

End point values	Elafibranor 120 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: number of subjects with event	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of adverse events

End point title	Incidence of adverse events

End point description:

End point type	Secondary

End point timeframe:

from signature of the subject ICF at the first Screening Visit until the end of study visit

End point values	Safety set			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: number of subjects with a least 1 event	12			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of treatment emergent adverse event

End point title	Incidence of treatment emergent adverse event

End point description:

End point type	Secondary

End point timeframe:

from signature of the subject ICF at the first Screening Visit until the end of study visit

End point values	Safety set			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: Number of subjects with at least 1 event	10			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of treatment emergent adverse events related to study treatment

End point title	Incidence of treatment emergent adverse events related to study treatment

End point description:

End point type	Secondary

End point timeframe:

from signature of the subject ICF at the first Screening Visit until the end of study visit

End point values	Safety set			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: Number of subjects with at least 1 event	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of treatment emergent adverse events related to study procedures

End point title	Incidence of treatment emergent adverse events related to study procedures

End point description:

End point type	Secondary

End point timeframe:

from signature of the subject ICF at the first Screening Visit until the end of study visit

End point values	Safety set			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: Number of subjects with at least 1 event	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of serious adverse events

End point title	Incidence of serious adverse events

End point description:

End point type	Secondary

End point timeframe:

from signature of the subject ICF at the first Screening Visit until the end of study visit

End point values	Safety set			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: Number of subjects with at least 1 event	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of serious treatment emergent adverse events

End point title	Incidence of serious treatment emergent adverse events

End point description:

End point type	Secondary

End point timeframe:

from signature of the subject ICF at the first Screening Visit until the end of study visit

End point values	Safety set			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: Number of subjects with at least 1 event	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of serious treatment emergent adverse events related to study treatment

End point title	Incidence of serious treatment emergent adverse events related to study treatment

End point description:

End point type	Secondary

End point timeframe:

from signature of the subject ICF at the first Screening Visit until the end of study visit

End point values	Safety set			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: Number of subjects with at least 1 event	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of serious treatment emergent adverse events related to study procedure

End point title	Incidence of serious treatment emergent adverse events related to study procedure

End point description:

End point type	Secondary

End point timeframe:

from signature of the subject ICF at the first Screening Visit until the end of study visit

End point values	Safety set			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: Number of subjects with at least 1 event	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of adverse events leading to treatment withdrawal

End point title	Incidence of adverse events leading to treatment withdrawal

End point description:

End point type	Secondary

End point timeframe:

from signature of the subject ICF at the first Screening Visit until the end of study visit

End point values	Safety set			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: Number of subjects with at least 1 event	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of treatment emergent adverse event leading to treatment withdrawal

End point title	Incidence of treatment emergent adverse event leading to treatment withdrawal

End point description:

End point type	Secondary

End point timeframe:

from signature of the subject ICF at the first Screening Visit until the end of study visit

End point values	Safety set			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: Number of subjects with at least 1 event	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of adverse events leading to study withdrawal

End point title	Incidence of adverse events leading to study withdrawal

End point description:

End point type	Secondary

End point timeframe:

from signature of the subject ICF at the first Screening Visit until the end of study visit

End point values	Safety set			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: Number of subjects with at least 1 event	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of treatment emergent adverse events leading to study withdrawal

End point title	Incidence of treatment emergent adverse events leading to study withdrawal

End point description:

End point type	Secondary

End point timeframe:

from signature of the subject ICF at the first Screening Visit until the end of study visit

End point values	Safety set			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: Number of subjects with at least 1 event	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of fatal adverse events

End point title	Incidence of fatal adverse events

End point description:

End point type	Secondary

End point timeframe:

from signature of the subject ICF at the first Screening Visit until the end of study visit

End point values	Safety set			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: Number of subjects with at least 1 event	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of fatal treatment emergent adverse event

End point title	Incidence of fatal treatment emergent adverse event

End point description:

End point type	Secondary

End point timeframe:

from signature of the subject ICF at the first Screening Visit until the end of study visit

End point values	Safety set			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: Number of subjects with at least 1 event	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of adverse events of special interest

End point title	Incidence of adverse events of special interest

End point description:

AESI are TEAEs corresponding to the conceptual definition of:
CPK elevations of severe intensity or leading to permanent study drug discontinuation;
Muscle injury symptoms of severe intensity corresponding to muscle pain or myalgia, Muscle spasms or tremor, muscle weakness;
Transaminases elevations from baseline of severe intensity or leading to permanent study drug discontinuation;
Liver injury events of severe intensity corresponding to hepatic impairment, hepatic failure;
Gastrointestinal symptoms of severe intensity corresponding to abdominal pain, constipation, diarrhea, nausea, vomiting, acute cholecystis, acute pancreatitis;
Fatigue and asthenia of severe intensity;
Serum creatinine elevations of severe intensity or leading to permanent study drug discontinuation;
Renal injury events of moderate or severe intensity corresponding to renal failure, renal impairment, renal colic.

End point type	Secondary

End point timeframe:

from signature of the subject ICF at the first Screening Visit until the end of study visit

End point values	Safety set			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: Number of subjects with at least 1 event	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of clinically significant change in smoking habits

End point title	Incidence of clinically significant change in smoking habits

End point description:

End point type	Secondary

End point timeframe:

from the first screening visit until Visit 6 of the second treatment period

End point values	Elafibranor 120 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: number of subjects with CS change	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

from signature of the subject ICF at the first Screening Visit until the end of study visit

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Overall population

Reporting group description: -

Serious adverse events	Overall population		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 17 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Overall population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 17 (70.59%)		
Investigations			
Blood glucose increased			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
C-reactive protein increased			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Vascular disorders			

Arterial disorder subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
General disorders and administration site conditions Chest discomfort subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1 1 / 17 (5.88%) 1		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Toothache subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1 1 / 17 (5.88%) 1		
Reproductive system and breast disorders Scrotal inflammation subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Laryngitis subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1 1 / 17 (5.88%) 1		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		

Infections and infestations			
Influenza			
subjects affected / exposed	3 / 17 (17.65%)		
occurrences (all)	3		
Nasopharyngitis			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Tooth infection			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 December 2019	The protocol was amended in order to add an analysis set and update a series of endpoints. The changes mainly concerned: Specification of a PP set to be included for analysis purposes; inclusion of renal function and anthropometry as objectives, in line with existing endpoints; medical history was removed as a safety objective and safety endpoints were presented in more detail; specification that whole body insulin sensitivity rather than glucose infusion rate at the end of 6 weeks of treatment would be assessed as an exploratory objective and endpoint, with details of assessment parameters included; specification that waist circumference was to be assessed at the end of each 6-week treatment period, rather than as change from baseline; clarification of various other endpoints.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
14 July 2020	Due to the COVID-19 pandemic, subjects had difficulty visiting the study site due to lockdown rules and travel restrictions, so the study was put on hold on 15 March 2019. The sponsor then decided to prematurely terminate this study on 14 July 2020 (IEC and Regulatory Authority notified on 14 August 2020) due to lack of efficacy, but not due to safety concerns, seen in the interim results from the Phase 3 RESOLVE-IT study in subjects with NASH published on 11 May 2020. As a result of this premature termination the remaining 11 subjects did not complete this study.	-

Notes:

Limitations and caveats

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

Due to the premature termination of this study no efficacy analyses were conducted since too few subjects completed both study periods. As such the efficacy objectives were not met and no conclusions can be drawn from the efficacy data.

Notes: