Clinical trial results:
An Open Label, Randomized, Multicenter Study to Assess the Pharmacokinetic and Pharmacodynamic Profile and the Safety and Tolerability of Two Dose Levels of Elafibranor (80 mg and 120 mg) in Children and Adolescents, 8 to 17 Years of Age, With Nonalcoholic Steatohepatitis (NASH)

Summary

EudraCT number	2019-003400-12
Trial protocol	Outside EU/EEA
Global end of trial date	16 June 2020

Results information

Result version number	v1 (current)
This version publication date	13 October 2021
First version publication date	13 October 2021

Trial information

Trial identification

Sponsor protocol code	GFT505E-218-1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03883607
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	Clinical Trials Contact Point, GENFIT, +01 6179536469, clinicaltrial@genfit.com
Scientific contact	Carol Addy, MD MMSc, Study Director, GENFIT, +01 6179536469, clinicaltrial@genfit.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001857-PIP01-15
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	16 June 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 June 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study was to assess the pharmacokinetics (PK) of elafibranor and its active metabolite GFT1007, following once daily oral administration of two dose levels of elafibranor (80 milligrams [mg] and 120 mg) to children and adolescents, 8 to 17 years of age (inclusive).

Protection of trial subjects:

This study was conducted in accordance with the principles laid down by the 18th World Medical Assembly (Helsinki, 1964) and all applicable amendments laid down by the World Medical Assemblies, and the Good Clinical Practice (GCP) guideline (CHMP, 2016). This study also complied with applicable local regulatory requirements and laws of each country in which the study was performed, as well as any applicable guidelines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 June 2019
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 States: 10
Worldwide total number of subjects	10
EEA total number of subjects	0

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)	10
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 2 centers in the United States from 25 June 2019 and 16 June 2020. A total of 27 subjects were screened, of which 10 subjects were enrolled and randomised (1:1 ratio) to receive elafibranor 80 mg/120 mg sequentially. A total of 17 subjects failed screening mainly due to not meeting eligibility criteria.

Pre-assignment

Screening details:

Screening was performed up to 4 weeks before study drug administered. Randomisation: stratified by age (Cohort 1: >=12 to <=17 years; Cohort 2: >=8 to <=11 years) and historical fibrosis severity stage (stratum 1:0 to 1; stratum 2:2 to 3). Due to lack of efficacy, study was prematurely terminated, only Cohort 1 subjects were involved in this study.

Period 1

Period 1 title	Overall Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Elafibranor 80 mg

Arm description:

Subjects received elafibranor 80 mg tablets orally once daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Elafibranor 80mg
Investigational medicinal product code	GFT505
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Elafibranor tablet orally once daily for 12 weeks.

Arm title	Elafibranor 120mg

Arm description:

Subjects received elafibranor 120 mg tablets orally once daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Elafibranor 120mg
Investigational medicinal product code	GFT505
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Elafibranor tablet orally once daily for 12 weeks.

Number of subjects in period 1	Elafibranor 80 mg	Elafibranor 120mg
Started	5	5
Completed	5	5

Baseline characteristics

Reporting groups	
Reporting group title	Elafibranor 80 mg
Reporting group description:	
Subjects received elafibranor 80 mg tablets orally once daily for 12 weeks.	
Reporting group title	Elafibranor 120mg
Reporting group description:	
Subjects received elafibranor 120 mg tablets orally once daily for 12 weeks.	

Reporting group values	Elafibranor 80 mg	Elafibranor 120mg	Total
Number of subjects	5	5	10
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	14.52	15.70	
standard deviation	± 2.23	± 2.31	-
Gender categorical Units: Subjects			
Female	0	0	0
Male	5	5	10
Ethnicity Units: Subjects			
Hispanic or Latino	4	5	9
Not Hispanic or Latino	1	0	1
Unknown or Not Reported	0	0	0
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	2	3	5
More than one race	0	0	0
Unknown or Not Reported	3	2	5

End points

End points reporting groups

Reporting group title	Elafibranor 80 mg
Reporting group description:	
Subjects received elafibranor 80 mg tablets orally once daily for 12 weeks.	
Reporting group title	Elafibranor 120mg
Reporting group description:	
Subjects received elafibranor 120 mg tablets orally once daily for 12 weeks.	

Primary: Pharmacokinetics: Maximum Observed Plasma Concentration (Cmax) of Elafibranor and its Active Metabolite (GFT1007)

End point title	Pharmacokinetics: Maximum Observed Plasma Concentration (Cmax) of Elafibranor and its Active Metabolite (GFT1007)[1]

End point description:

Cmax was defined as maximum observed plasma concentration. Analysis was performed on PK population that included all subjects who had received at least 1 dose of the study drug, did not had protocol deviations or adverse events (AEs) that significantly affected the PK, and had at least 1 post-dose PK sample.

End point type	Primary

End point timeframe:

Day 1: at pre-dose; Day 29: at pre-dose, 0.5, 1, 1.5, 2, 4, 6, 8 hours post-dose; Day 30 and 85: at 24 hours after previous day dose administration

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: Descriptive statistics were performed; no inferential statistical analyses were performed.

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Elafibranor	385.216 (± 218.646)	658.054 (± 403.201)		
GFT1007	2367.620 (± 1088.123)	2875.280 (± 1443.324)		

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetics: Time to Maximum Observed Plasma Concentration (Tmax) of Elafibranor and Active Metabolite (GFT1007)

End point title	Pharmacokinetics: Time to Maximum Observed Plasma Concentration (Tmax) of Elafibranor and Active Metabolite (GFT1007)[2]

End point description:

Tmax was defined as time to reach maximum observed plasma concentration. Analysis was performed

on PK population.

End point type	Primary

End point timeframe:

Day 1: at pre-dose; Day 29: at pre-dose, 0.5, 1, 1.5, 2, 4, 6, 8 hours post-dose; Day 30 and 85: at 24 hours after previous day dose administration

Notes:

[2] - 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: Descriptive statistics were performed; no inferential statistical analyses were performed.

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: hours				
median (full range (min-max))				
Elafibranor	1.50 (0.52 to 2.00)	1.00 (0.98 to 1.50)		
GFT1007	2.00 (1.50 to 2.00)	1.50 (1.00 to 1.50)		

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetics: Area Under The Plasma Concentration-time Curve From 0 to 24 Hours (AUC0-24) of Elafibranor and Active Metabolite (GFT1007)

End point title	Pharmacokinetics: Area Under The Plasma Concentration-time Curve From 0 to 24 Hours (AUC0-24) of Elafibranor and Active Metabolite (GFT1007)[3]

End point description:

AUC0-24 was defined as the area under the plasma concentration versus time curve of the study drug from time 0 to 24 hours. Analysis was performed on PK population.

End point type	Primary

End point timeframe:

Day 1: at pre-dose; Day 29: at pre-dose, 0.5, 1, 1.5, 2, 4, 6, 8 hours post-dose; Day 30 and 85: at 24 hours after previous day dose administration

Notes:

[3] - 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: Descriptive statistics were performed; no inferential statistical analyses were performed.

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: nanograms*hour per milliliter				
arithmetic mean (standard deviation)				
Elafibranor	973.301 (± 311.803)	1457.728 (± 724.018)		
GFT1007	10011.405 (± 3575.220)	10532.930 (± 3257.220)		

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetics: Terminal Elimination Half-life (t½) of Elafibranor and Active Metabolite (GFT1007)

End point title	Pharmacokinetics: Terminal Elimination Half-life (t½) of Elafibranor and Active Metabolite (GFT1007)[4]

End point description:

Plasma t1/2 was defined as the time taken by drug to reduce to half of its initial plasma concentration. Analysis was performed on PK population. Here, "n= number analysed" signifies those subjects who were evaluable for specified category. Here, '99999' indicates that standard deviation was not estimated as only single subject was analysed for the each specified category.

End point type	Primary

End point timeframe:

Day 1: at pre-dose; Day 29: at pre-dose, 0.5, 1, 1.5, 2, 4, 6, 8 hours post-dose; Day 30 and 85: at 24 hours after previous day dose administration

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: Descriptive statistics were performed; no inferential statistical analyses were performed.

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: hours				
arithmetic mean (standard deviation)				
Elafibranor (n= 1, 3)	34.170 (± 99999)	37.620 (± 15.473)		
GFT1007 (n=4, 5)	9.572 (± 5.592)	6.682 (± 1.120)		

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetics: Plasma Trough Concentrations (Ctrough) of Elafibranor and Active Metabolite (GFT1007)

End point title	Pharmacokinetics: Plasma Trough Concentrations (Ctrough) of Elafibranor and Active Metabolite (GFT1007)[5]

End point description:

Ctrough was defined as the plasma concentration of study drug observed just before treatment administration during repeated dosing. Analysis was performed on PK population.

End point type	Primary

End point timeframe:

Pre-dose on Day 1 and 29

Notes:

[5] - 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: Descriptive statistics were performed; no inferential statistical analyses were performed.

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: ng/mL				
arithmetic mean (standard deviation)				
Elafibranor	14.904 (± 3.516)	29.035 (± 15.087)		
GFT1007	97.771 (± 49.636)	55.243 (± 27.769)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics (PD) - Liver Markers: Change From Baseline in Serum Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Gamma-glutamyl Transferase (GGT), and Alkaline Phosphatase (ALP) at Days 15, 29, 57, 85 and 113

End point title	Pharmacodynamics (PD) - Liver Markers: Change From Baseline in Serum Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Gamma-glutamyl Transferase (GGT), and Alkaline Phosphatase (ALP) at Days 15, 29, 57, 85 and 113

End point description:

Baseline was defined as the last measurement before first intake of study treatment on Day 1. Missing data were not imputed for the analysis. Normal range at screening: AST: 0 - 39 international units per liter (IU/L), ALT: 5 - 30 IU/L, GGT: 2 - 24 IU/L, and ALP: 74 - 390 IU/L. Analysis was performed on intent-to-treat (ITT) population that had included subjects who were randomised and had received at least 1 dose of the study drug. Here, "n= number analysed" signifies those subjects who were evaluable for each specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 15, 29, 57, 85 and 113

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: IU/L				
arithmetic mean (standard deviation)				
ALT: Day 15 (n= 5, 5)	4.2 (± 21.7)	-13.8 (± 25.0)		
ALT: Day 29 (n= 5, 5)	-0.2 (± 35.9)	-27.6 (± 18.4)		
ALT: Day 57 (n= 5, 5)	0.2 (± 27.3)	-30.8 (± 16.5)		
ALT: Day 85 (n= 5, 5)	17.8 (± 56.6)	-34.6 (± 25.6)		

ALT: Day 113 (n= 4, 4)	37.3 (± 46.9)	-28.0 (± 22.2)		
AST: Day 15 (n= 5, 5)	4.0 (± 16.0)	0.8 (± 9.5)		
AST: Day 29 (n= 5, 5)	4.0 (± 16.3)	-4.0 (± 9.5)		
AST: Day 57 (n= 5, 5)	1.0 (± 6.1)	-5.8 (± 4.1)		
AST: Day 85 (n= 5, 5)	7.4 (± 15.3)	-8.2 (± 8.3)		
AST: Day 113 (n= 4, 4)	9.3 (± 8.4)	-7.8 (± 8.7)		
GGT: Day 15 (n= 5, 5)	-9.2 (± 6.8)	-8.8 (± 4.4)		
GGT: Day 29 (n= 5, 5)	-15.6 (± 9.9)	-16.0 (± 5.9)		
GGT: Day 57 (n= 5, 5)	-1.0 (± 20.7)	-15.6 (± 9.1)		
GGT: Day 85 (n= 5, 5)	11.2 (± 39.1)	-16.2 (± 9.9)		
GGT: Day 113 (n= 4, 4)	45.3 (± 43.8)	-9.5 (± 6.6)		
ALP: Day 15 (n= 5, 5)	-4.6 (± 23.1)	-18.0 (± 11.2)		
ALP: Day 29 (n= 5, 5)	-24.8 (± 28.4)	-14.6 (± 8.1)		
ALP: Day 57 (n = 5, 5)	-28.2 (± 36.5)	-18.4 (± 8.2)		
ALP: Day 85 (n= 5, 5)	-32.6 (± 51.5)	-25.0 (± 12.4)		
ALP: Day 113 (n =4, 4)	-7.8 (± 45.4)	-16.8 (± 10.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics - Other Liver Markers: Change From Baseline in Adiponectin at Days 29, 57, 85 and 113

End point title	Pharmacodynamics - Other Liver Markers: Change From Baseline in Adiponectin at Days 29, 57, 85 and 113

End point description:

Baseline was defined as the last measurement before first intake of study treatment on Day 1. Missing data were not imputed for the analysis. Analysis was performed on ITT population. Here, "n= number analysed" signifies those subjects who were evaluable for each specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 29, 57, 85 and 113

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: micrograms per milliliter (mcg/mL)				
arithmetic mean (standard deviation)				
Day 29 (n= 5, 5)	0.2410 (± 0.3729)	0.2112 (± 1.0304)		
Day 57 (n= 5, 5)	0.5780 (± 1.0530)	-0.2752 (± 1.0022)		
Day 85 (n= 5, 5)	0.3372 (± 1.4844)	-0.0590 (± 1.0476)		
Day 113 (n= 4, 4)	-0.4663 (± 0.8972)	0.0322 (± 1.0588)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics - Other Liver Markers: Change From Baseline in Cytokeratin 18 (CK-18)/M65 and CK-18/M30 at Days 29, 57, 85 and 113

End point title	Pharmacodynamics - Other Liver Markers: Change From Baseline in Cytokeratin 18 (CK-18)/M65 and CK-18/M30 at Days 29, 57, 85 and 113

End point description:

Baseline was defined as the last measurement before first intake of study treatment on Day 1. Missing data were not imputed for the analysis. Analysis was performed on ITT population. Here, "n= number analysed" signifies those subjects who were evaluable for each specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 29, 57, 85 and 113

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: IU/L				
arithmetic mean (standard deviation)				
CK-18/M65: Day 29 (n= 5, 5)	39.412 (± 346.370)	-70.902 (± 121.905)		
CK-18/M65: Day 57 (n= 5, 5)	-30.302 (± 326.632)	-60.578 (± 186.165)		
CK-18/M65: Day 85 (n= 5, 5)	-2.320 (± 231.775)	-122.070 (± 265.059)		
CK-18/M65: Day 113 (n= 4, 4)	235.205 (± 290.846)	-188.638 (± 244.324)		
CK-18/M30: Day 29 (n= 5, 5)	-24.282 (± 374.146)	-68.896 (± 96.850)		
CK-18/M30: Day 57 (n= 5, 5)	7.530 (± 445.509)	-20.074 (± 219.782)		
CK-18/M30: Day 85 (n= 5, 5)	-54.988 (± 315.261)	-81.492 (± 271.506)		
CK-18/M30: Day 113 (n= 4, 4)	146.412 (± 273.673)	-170.793 (± 235.722)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics - Other Liver Markers: Change From Baseline in Ferritin at Days 29, 57, 85 and 113

End point title	Pharmacodynamics - Other Liver Markers: Change From Baseline in Ferritin at Days 29, 57, 85 and 113

End point description:

Baseline was defined as the last measurement before first intake of study treatment on Day 1. Missing data were not imputed for the analysis. Analysis was performed on ITT population. Here, "n= number analysed" signifies those subjects who were evaluable for each specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 29, 57, 85 and 113

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: micrograms per liter (mcg/L)				
arithmetic mean (standard deviation)				
Day 29 (n= 5, 5)	6.4 (± 12.0)	10.8 (± 25.9)		
Day 57 (n= 5, 5)	19.4 (± 23.5)	3.6 (± 15.6)		
Day 85 (n= 5, 5)	11.8 (± 16.6)	-4.0 (± 2.4)		
Day 113 (n= 4, 4)	6.0 (± 5.7)	-12.8 (± 11.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics - Other Liver Markers: Change From Baseline in Fibroblast Growth Factor 19 and Fibroblast Growth Factor 21 at Days 29, 57, 85 and 113

End point title	Pharmacodynamics - Other Liver Markers: Change From Baseline in Fibroblast Growth Factor 19 and Fibroblast Growth Factor 21 at Days 29, 57, 85 and 113

End point description:

Baseline was defined as the last measurement before first intake of study treatment on Day 1. Missing data were not imputed for the analysis. Analysis was performed on ITT population. Here, "n= number analysed" signifies those subjects who were evaluable for specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 29, 57, 85 and 113

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: picograms per milliliter (pg/mL)				
arithmetic mean (standard deviation)				
Fibroblast Growth Factor 19: Day 29 (n= 5, 5)	-24.4 (± 80.6)	-42.8 (± 78.0)		
Fibroblast Growth Factor 19: Day 57 (n= 5, 5)	-10.4 (± 51.2)	-18.8 (± 85.3)		
Fibroblast Growth Factor 19: Day 85 (n= 5, 5)	28.4 (± 77.5)	-13.0 (± 100.6)		
Fibroblast Growth Factor 19: Day 113 (n= 4, 4)	-7.8 (± 61.3)	-19.8 (± 35.3)		
Fibroblast Growth Factor 21: Day 29 (n= 5, 5)	9.98 (± 91.38)	128.84 (± 171.50)		
Fibroblast Growth Factor 21: Day 57 (n= 5, 5)	-36.36 (± 188.91)	195.94 (± 315.73)		
Fibroblast Growth Factor 21: Day 85 (n= 5, 5)	120.68 (± 191.62)	81.56 (± 130.68)		
Fibroblast Growth Factor 21: Day 113 (n= 4, 4)	3.50 (± 291.41)	56.35 (± 87.53)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics - Other Liver Markers: Change From Baseline in Hyaluronic Acid, Procollagen 3 N-Terminal Propeptide (PIIINP) and Tissue Inhibitor of Metalloproteinase 1 (TIMP1) at Days 29, 57, 85 and 113

End point title	Pharmacodynamics - Other Liver Markers: Change From Baseline in Hyaluronic Acid, Procollagen 3 N-Terminal Propeptide (PIIINP) and Tissue Inhibitor of Metalloproteinase 1 (TIMP1) at Days 29, 57, 85 and 113

End point description:

Baseline was defined as the last measurement before first intake of study treatment on Day 1. Missing data were not imputed for the analysis. Analysis was performed on ITT population. Here, "n= number analysed" signifies those subjects who were evaluable for each specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 29, 57, 85 and 113

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Hyaluronic Acid: Day 29 (n= 5, 5)	-2.958 (± 11.689)	-8.800 (± 10.991)		
Hyaluronic Acid: Day 57 (n= 5, 5)	-0.272 (± 9.228)	-3.654 (± 10.528)		

Hyaluronic Acid: Day 85 (n= 5, 5)	4.408 (± 16.612)	-3.518 (± 15.130)		
Hyaluronic Acid: Day 113 (n= 4, 4)	1.592 (± 16.445)	-0.422 (± 19.347)		
PIIINP: Day 29 (n= 5, 5)	-3.018 (± 14.079)	-2.878 (± 3.138)		
PIIINP: Day 57 (n= 5, 5)	1.730 (± 6.928)	-2.762 (± 3.242)		
PIIINP: Day 85 (n= 5, 5)	-1.710 (± 6.730)	-0.470 (± 5.270)		
PIIINP: Day 113 (n= 4, 4)	-7.015 (± 11.902)	-0.530 (± 3.701)		
TIMP1: Day 29 (n= 5, 5)	-3.56 (± 25.38)	-8.52 (± 8.98)		
TIMP1: Day 57 (n= 5, 5)	2.80 (± 15.35)	-26.20 (± 32.29)		
TIMP1: Day 85 (n= 5, 5)	16.02 (± 24.84)	-26.26 (± 25.43)		
TIMP1: Day 113 (n= 4, 4)	10.92 (± 21.58)	-31.35 (± 37.95)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics - Other Liver Markers: Change From Baseline in Alpha-2 Macroglobulin at Days 29, 57, 85 and 113

End point title	Pharmacodynamics - Other Liver Markers: Change From Baseline in Alpha-2 Macroglobulin at Days 29, 57, 85 and 113

End point description:

Baseline was defined as the last measurement before first intake of study treatment on Day 1. Missing data were not imputed for the analysis. Analysis was performed on ITT population. Here, "n= number analysed" signifies those subjects who were evaluable for each specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 29, 57, 85 and 113

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: gram per liter (g/L)				
arithmetic mean (standard deviation)				
Day 29 (n= 5, 5)	-0.098 (± 0.254)	-0.282 (± 0.133)		
Day 57 (n= 5, 5)	0.124 (± 0.213)	-0.118 (± 0.064)		
Day 85 (n= 5, 5)	-0.030 (± 0.328)	-0.204 (± 0.129)		
Day 113 (n= 4, 4)	-0.105 (± 0.319)	-0.037 (± 0.157)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics - Glucose Homeostasis Markers: Change From Baseline in Fasting Plasma Glucose (FPG) at Days 15, 29, 57, 85 and 113

End point title	Pharmacodynamics - Glucose Homeostasis Markers: Change From Baseline in Fasting Plasma Glucose (FPG) at Days 15, 29, 57, 85 and 113

End point description:

Blood samples were taken after minimum 10 hours of fasting. Baseline was defined as the last measurement before first intake of study treatment on Day 1. Analysis was performed on ITT population. Here, "n= number analysed" signifies those subjects who were evaluable for each specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 15, 29, 57, 85 and 113

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)				
Day 15 (n= 5, 5)	0.22 (± 0.34)	0.22 (± 0.28)		
Day 29 (n= 5, 5)	0.34 (± 0.61)	0.12 (± 0.47)		
Day 57 (n= 5, 4)	0.18 (± 0.58)	0.10 (± 0.24)		
Day 85 (n= 5, 5)	0.28 (± 0.63)	0.08 (± 0.45)		
Day 113 (n= 4, 4)	0.58 (± 0.52)	0.17 (± 0.35)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics - Glucose Homeostasis Markers: Change From Baseline in Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) at Days 15, 29, 57, 85 and 113

End point title	Pharmacodynamics - Glucose Homeostasis Markers: Change From Baseline in Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) at Days 15, 29, 57, 85 and 113

End point description:

HOMA IR measures insulin resistance based on fasting glucose and insulin measurements: HOMA IR = fasting plasma insulin (micro international units per milliliter [mcIU/mL]) * fasting plasma glucose

(mmol/L) / 22.5. A higher value indicates a greater insulin resistance. Baseline was defined as the last measurement before first intake of study treatment on Day 1. Analysis was performed on ITT population. Here, "n= number analysed" signifies those subjects who were evaluable for each specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 15, 29, 57, 85 and 113

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: Insulin resistance				
arithmetic mean (standard deviation)				
Day 15 (n= 5, 5)	10.720 (± 17.650)	-3.640 (± 5.215)		
Day 29 (n= 5, 5)	16.498 (± 43.577)	-4.028 (± 6.512)		
Day 57 (n= 5, 4)	4.958 (± 15.472)	-5.448 (± 3.572)		
Day 85 (n= 5, 5)	3.742 (± 6.853)	-1.968 (± 7.112)		
Day 113 (n= 4, 4)	13.323 (± 22.795)	-4.623 (± 6.883)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics - Glucose Homeostasis Markers: Change From Baseline in Fasting Insulin at Days 15, 29, 57, 85 and 113

End point title	Pharmacodynamics - Glucose Homeostasis Markers: Change From Baseline in Fasting Insulin at Days 15, 29, 57, 85 and 113

End point description:

Blood samples were taken after minimum 10 hours of fasting. Baseline was defined as the last measurement before first intake of study treatment on Day 1. Analysis was performed on ITT population. Here, "n= number analysed" signifies those subjects who were evaluable for each specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 15, 29, 57, 85 and 113

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: milli-international unit per liter				
arithmetic mean (standard deviation)				
Day 15 (n= 5, 5)	30.88 (± 53.53)	-15.66 (± 20.92)		
Day 29 (n= 5, 5)	40.12 (± 116.20)	-16.76 (± 24.12)		
Day 57 (n= 5, 4)	12.42 (± 41.76)	-23.10 (± 12.58)		
Day 85 (n= 5, 5)	9.70 (± 15.49)	-7.48 (± 26.76)		
Day 113 (n= 4, 4)	34.15 (± 58.20)	-19.57 (± 25.56)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics - Serum Lipid Parameters: Change From Baseline in Serum Total Cholesterol (TC) at Days 15, 29, 57, 85 and 113

End point title	Pharmacodynamics - Serum Lipid Parameters: Change From Baseline in Serum Total Cholesterol (TC) at Days 15, 29, 57, 85 and 113

End point description:

Baseline was defined as the last measurement before first intake of study treatment on Day 1. Analysis was performed on ITT population. Here, "n= number analysed" signifies those subjects who were evaluable for each specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 15, 29, 57, 85 and 113

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: mmol/L				
arithmetic mean (standard deviation)				
Day 15 (n= 5, 5)	-0.070 (± 0.440)	-0.328 (± 0.230)		
Day 29 (n= 5, 5)	-0.356 (± 0.252)	-0.288 (± 0.347)		
Day 57 (n= 5, 5)	0.380 (± 0.565)	-0.286 (± 0.129)		
Day 85 (n= 5, 5)	0.298 (± 0.836)	-0.274 (± 0.306)		
Day 113 (n= 4, 4)	0.665 (± 0.919)	0.105 (± 0.270)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics - Serum Lipid Parameters: Change From Baseline in Serum Non High-density Lipoprotein Cholesterol (Non-HDL-C) at Days 15, 29, 57, 85 and 113

End point title	Pharmacodynamics - Serum Lipid Parameters: Change From Baseline in Serum Non High-density Lipoprotein Cholesterol (Non-HDL-C) at Days 15, 29, 57, 85 and 113

End point description:

Baseline was defined as the last measurement before first intake of study treatment on Day 1. Analysis was performed on ITT population. Here, "n= number analysed" signifies those subjects who were evaluable for each specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 15, 29, 57, 85 and 113

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: mmol/L				
arithmetic mean (standard deviation)				
Day 15 (n= 5, 5)	-0.134 (± 0.414)	-0.348 (± 0.163)		
Day 29 (n= 5, 5)	-0.324 (± 0.196)	-0.316 (± 0.432)		
Day 57 (n= 5, 5)	0.368 (± 0.340)	-0.316 (± 0.194)		
Day 85 (n= 5, 5)	0.156 (± 0.615)	-0.420 (± 0.290)		
Day 113 (n= 4, 4)	0.605 (± 0.714)	-0.038 (± 0.229)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics - Serum Lipid Parameters: Change From Baseline in Serum High-density Lipoprotein Cholesterol (HDL-C) at Days 15, 29, 57, 85 and 113

End point title	Pharmacodynamics - Serum Lipid Parameters: Change From Baseline in Serum High-density Lipoprotein Cholesterol (HDL-C) at Days 15, 29, 57, 85 and 113

End point description:

Baseline was defined as the last measurement before first intake of study treatment on Day 1. Analysis was performed on ITT population. Here, "n= number analysed" signifies those subjects who were evaluable for each specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 15, 29, 57, 85 and 113

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: mmol/L				
arithmetic mean (standard deviation)				
Day 15 (n= 5, 5)	0.060 (± 0.068)	0.020 (± 0.223)		
Day 29 (n= 5, 5)	-0.032 (± 0.124)	0.032 (± 0.137)		
Day 57 (n= 5, 5)	0.008 (± 0.228)	0.030 (± 0.168)		
Day 85 (n= 5, 5)	0.138 (± 0.278)	0.150 (± 0.191)		
Day 113 (n= 4, 4)	0.065 (± 0.259)	0.150 (± 0.047)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics - Serum Lipid Parameters: Change From Baseline in Serum Low-density Lipoprotein (LDL-C) at Days 15, 29, 57, 85 and 113

End point title	Pharmacodynamics - Serum Lipid Parameters: Change From Baseline in Serum Low-density Lipoprotein (LDL-C) at Days 15, 29, 57, 85 and 113

End point description:

Baseline was defined as the last measurement before first intake of study treatment on Day 1. Analysis was performed on ITT population. Here, "n= number analysed" signifies those subjects who were evaluable for each specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 15, 29, 57, 85 and 113

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: mmol/L				
arithmetic mean (standard deviation)				
Day 15 (n= 5, 5)	-0.224 (± 0.365)	-0.084 (± 0.213)		
Day 29 (n= 5, 5)	-0.344 (± 0.184)	-0.076 (± 0.355)		
Day 57 (n= 5, 5)	0.314 (± 0.355)	-0.038 (± 0.078)		
Day 85 (n= 5, 5)	0.080 (± 0.686)	-0.184 (± 0.223)		
Day 113 (n= 4, 4)	0.385 (± 0.691)	0.108 (± 0.134)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics - Serum Lipid Parameters: Change From Baseline in Serum Triglycerides at Days 15, 29, 57, 85 and 113

End point title	Pharmacodynamics - Serum Lipid Parameters: Change From Baseline in Serum Triglycerides at Days 15, 29, 57, 85 and 113

End point description:

Baseline was defined as the last measurement before first intake of study treatment on Day 1. Analysis was performed on ITT population. Here, "n= number analysed" signifies those subjects who were evaluable for each specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 15, 29, 57, 85 and 113

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: mmol/L				
arithmetic mean (standard deviation)				
Day 15 (n= 5, 5)	0.200 (± 0.363)	-0.576 (± 0.442)		
Day 29 (n= 5, 5)	0.042 (± 0.214)	-0.530 (± 0.385)		
Day 57 (n= 5, 5)	0.124 (± 0.326)	-0.606 (± 0.384)		
Day 85 (n= 5, 5)	0.170 (± 0.389)	-0.532 (± 0.399)		
Day 113 (n= 4, 4)	0.485 (± 0.918)	-0.315 (± 0.353)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics - Serum Lipid Parameters: Change From Baseline in Serum Calculated Very Low-density Lipoprotein Cholesterol (VLDL-C) at Days 15, 29, 57, 85 and 113

End point title	Pharmacodynamics - Serum Lipid Parameters: Change From Baseline in Serum Calculated Very Low-density Lipoprotein Cholesterol (VLDL-C) at Days 15, 29, 57, 85 and 113

End point description:

Baseline was defined as the last measurement before first intake of study treatment on Day 1. Analysis was performed on ITT population. Here, "n= number analysed" signifies those subjects who were evaluable for each specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 15, 29, 57, 85 and 113

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: mmol/L				
arithmetic mean (standard deviation)				
Day 15 (n= 5, 5)	0.086 (± 0.172)	-0.270 (± 0.200)		
Day 29 (n= 5, 5)	0.018 (± 0.103)	-0.244 (± 0.168)		
Day 57 (n= 5, 5)	0.052 (± 0.140)	-0.282 (± 0.176)		
Day 85 (n= 5, 5)	0.072 (± 0.168)	-0.240 (± 0.176)		
Day 113 (n= 4, 4)	0.215 (± 0.419)	-0.153 (± 0.156)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics - Serum Lipid Parameters: Change From Baseline in Serum Apolipoprotein A-1 at Days 15, 29, 57, 85 and 113

End point title	Pharmacodynamics - Serum Lipid Parameters: Change From Baseline in Serum Apolipoprotein A-1 at Days 15, 29, 57, 85 and 113

End point description:

Baseline was defined as the last measurement before first intake of study treatment on Day 1. Analysis was performed on ITT population. Here, "n= number analysed" signifies those subjects who were evaluable for each specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 15, 29, 57, 85 and 113

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: grams per liter (g/L)				
arithmetic mean (standard deviation)				
Day 15 (n= 5, 5)	0.112 (± 0.129)	-0.058 (± 0.149)		
Day 29 (n= 5, 5)	0.012 (± 0.139)	-0.058 (± 0.144)		
Day 57 (n= 5, 5)	0.108 (± 0.211)	-0.060 (± 0.176)		
Day 85 (n= 5, 5)	0.128 (± 0.268)	0.016 (± 0.160)		
Day 113 (n= 4, 4)	0.103 (± 0.313)	0.048 (± 0.060)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics - Serum Lipid Parameters: Change From Baseline in Serum Apolipoprotein B at Days 15, 29, 57, 85 and 113

End point title	Pharmacodynamics - Serum Lipid Parameters: Change From Baseline in Serum Apolipoprotein B at Days 15, 29, 57, 85 and 113

End point description:

Baseline was defined as the last measurement before first intake of study treatment on Day 1. Analysis was performed on ITT population. Here, "n= number analysed" signifies those subjects who were evaluable for each specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 15, 29, 57, 85 and 113

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: g/L				
arithmetic mean (standard deviation)				
Day 15 (n= 5, 5)	-0.058 (± 0.064)	-0.082 (± 0.074)		
Day 29 (n= 5, 5)	-0.098 (± 0.081)	-0.078 (± 0.097)		
Day 57 (n= 5, 5)	0.066 (± 0.092)	-0.062 (± 0.086)		
Day 85 (n= 5, 5)	0.020 (± 0.189)	-0.036 (± 0.090)		
Day 113 (n= 4, 4)	0.117 (± 0.209)	-0.005 (± 0.135)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics - Change From Baseline in Body Weight at Days 15, 29, 57, 85 and 113

End point title	Pharmacodynamics - Change From Baseline in Body Weight at Days 15, 29, 57, 85 and 113

End point description:

Baseline was defined as the last measurement before first intake of study treatment on Day 1. Analysis was performed on ITT population. Here, "n= number analysed" signifies those subjects who were evaluable for each specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 15, 29, 57, 85 and 113

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: kilograms (kg)				
arithmetic mean (standard deviation)				
Day 15 (n= 5, 5)	-0.08 (± 3.03)	-0.92 (± 1.70)		
Day 29 (n= 5, 5)	-0.32 (± 4.54)	-0.98 (± 2.06)		
Day 57 (n= 5, 5)	0.73 (± 5.18)	-0.68 (± 3.27)		
Day 85 (n= 5, 5)	1.54 (± 5.42)	0.24 (± 4.07)		
Day 113 (n= 4, 5)	4.40 (± 3.05)	0.73 (± 4.63)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics - Change From Baseline in Body Mass Index (BMI) Z-Score at Days 15, 29, 57, 85 and 113

End point title	Pharmacodynamics - Change From Baseline in Body Mass Index (BMI) Z-Score at Days 15, 29, 57, 85 and 113

End point description:

The BMI for a given age (in years) and gender (male) was converted to an exact z-score. Given a subject's age, sex, BMI, and an appropriate reference standard, a BMI Z-score (also referred to as BMI-for-age percentile) was determined. BMI Z-score >=85th percentile was considered as overweight. Z-score was a statistical measure to describe whether a mean was above or below the standard. A Z-score of 0 was equal to the mean and is considered normal. Negative numbers indicate values lower than the mean and positive numbers indicate values higher than the mean. Negative values are indicative of decrease in BMI (weight loss) and positive values are indicative of increase in BMI. Baseline was defined as the last measurement before first intake of study treatment on Day 1. Analysis was performed on ITT population. Here, "n= number analysed" signifies those subjects who were evaluable for specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 15, 29, 57, 85 and 113

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: Z-Score				
arithmetic mean (standard deviation)				
Day 15 (n= 5, 5)	-0.064 (± 0.146)	-0.054 (± 0.095)		
Day 29 (n= 5, 5)	-0.091 (± 0.247)	-0.054 (± 0.110)		
Day 57 (n= 5, 5)	-0.108 (± 0.284)	-0.058 (± 0.162)		
Day 85 (n= 5, 5)	-0.074 (± 0.290)	-0.026 (± 0.197)		
Day 113 (n= 4, 4)	0.068 (± 0.116)	0.022 (± 0.247)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics - Change From Baseline in Waist Circumference at Days 15, 29, 57, 85 and 113

End point title	Pharmacodynamics - Change From Baseline in Waist Circumference at Days 15, 29, 57, 85 and 113

End point description:

Waist circumference (in centimeters [cm]) was measured at the midpoint between the lower margin of the least palpable rib and the top of the iliac crest. Baseline was defined as the last measurement before first intake of study treatment on Day 1. Analysis was performed on ITT population. Here, "n= number analysed" signifies those subjects who were evaluable for specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 15, 29, 57, 85 and 113

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: cm				
arithmetic mean (standard deviation)				
Day 15 (n= 5, 5)	-1.056 (± 2.953)	-0.998 (± 2.961)		
Day 29 (n= 5, 5)	-0.656 (± 3.654)	-2.010 (± 2.625)		
Day 57 (n= 5, 5)	-0.316 (± 3.520)	-2.054 (± 4.106)		
Day 85 (n= 5, 5)	0.252 (± 3.379)	-1.346 (± 3.894)		
Day 113 (n= 4, 4)	1.625 (± 2.394)	-0.580 (± 4.099)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics - Inflammatory Marker: Change From Baseline in Fibrinogen at Days 29, 57, 85 and 113

End point title	Pharmacodynamics - Inflammatory Marker: Change From Baseline in Fibrinogen at Days 29, 57, 85 and 113

End point description:

Blood samples to assess fibrinogen levels were taken after minimum 10 hours of fasting. Baseline was defined as the last measurement before first intake of study treatment on Day 1. Analysis was performed on ITT population. Here, "n= number analysed" signifies those subjects who were evaluable for specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 29, 57, 85 and 113

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: micromoles per liter (mcmol/L)				
arithmetic mean (standard deviation)				
Day 29 (n= 5, 5)	-1.450 (± 1.265)	-2.474 (± 1.418)		
Day 57 (n= 5, 5)	-0.524 (± 1.309)	-2.220 (± 0.756)		

Day 85 (n= 5, 5)	-1.340 (± 1.492)	-1.748 (± 1.000)		
Day 113 (n= 4, 4)	-0.295 (± 1.936)	-1.150 (± 1.841)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics - Inflammatory Marker: Change From Baseline in Haptoglobin at Days 29, 57, 85 and 113

End point title	Pharmacodynamics - Inflammatory Marker: Change From Baseline in Haptoglobin at Days 29, 57, 85 and 113

End point description:

Blood samples to assess Haptoglobin level were taken after minimum 10 hours of fasting. Baseline was defined as the last measurement before first intake of study treatment on Day 1. Analysis was performed on ITT population. Here, "n= number analysed" signifies those subjects who were evaluable for specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 29, 57, 85 and 113

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: g/L				
arithmetic mean (standard deviation)				
Day 29 (n= 5, 5)	-0.086 (± 0.102)	-0.350 (± 0.244)		
Day 57 (n= 5, 5)	0.068 (± 0.118)	-0.300 (± 0.209)		
Day 85 (n= 5, 5)	0.066 (± 0.077)	-0.298 (± 0.236)		
Day 113 (n= 4, 4)	0.178 (± 0.208)	-0.058 (± 0.081)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics - Inflammatory Marker: Change From Baseline in Interleukin-6 at Days 29, 57, 85 and 113

End point title	Pharmacodynamics - Inflammatory Marker: Change From Baseline in Interleukin-6 at Days 29, 57, 85 and 113

End point description:

Blood samples to assess Interleukin-6 level were taken after minimum 10 hours of fasting. Baseline was defined as the last measurement before first intake of study treatment on Day 1. Analysis was performed on ITT population. Here, "n= number analysed" signifies those subjects who were evaluable

for specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 29, 57, 85 and 113

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: picograms per milliliter (pg/mL)				
arithmetic mean (standard deviation)				
Day 29 (n= 5, 5)	0.036 (± 0.080)	0.142 (± 0.751)		
Day 57 (n= 5, 5)	0.100 (± 0.224)	-0.092 (± 1.096)		
Day 85 (n= 5, 5)	0.142 (± 0.243)	0.062 (± 0.809)		
Day 113 (n= 4, 4)	0.143 (± 0.285)	0.078 (± 0.534)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics - Inflammatory Marker: Change From Baseline in Tumor Necrosis Factor Alpha at Days 29, 57, 85 and 113

End point title	Pharmacodynamics - Inflammatory Marker: Change From Baseline in Tumor Necrosis Factor Alpha at Days 29, 57, 85 and 113

End point description:

Blood samples to assess Necrosis Factor Alpha level were taken after minimum 10 hours of fasting. Baseline was defined as the last measurement before first intake of study treatment on Day 1. Analysis was performed on ITT population. Here, "n= number analysed" signifies those subjects who were evaluable for specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 29, 57, 85 and 113

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: pg/mL				
arithmetic mean (standard deviation)				
Day 29 (n= 5, 5)	-0.134 (± 0.437)	-0.460 (± 0.857)		
Day 57 (n= 5, 5)	0.068 (± 0.388)	-0.270 (± 0.651)		

Day 85 (n= 5, 5)	-0.068 (± 0.416)	-0.622 (± 0.939)		
Day 113 (n= 4, 4)	0.163 (± 0.534)	-0.445 (± 0.988)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics - Inflammatory Marker: Change From Baseline in Plasminogen Activator Inhibitor-1 at Days 29, 57, 85, and 113

End point title	Pharmacodynamics - Inflammatory Marker: Change From Baseline in Plasminogen Activator Inhibitor-1 at Days 29, 57, 85, and 113

End point description:

Blood samples to assess Plasminogen Activator Inhibitor-1 level were taken after minimum 10 hours of fasting. Baseline was defined as the last measurement before first intake of study treatment on Day 1. Analysis was performed on ITT population. Here, "n= number analysed" signifies those subjects who were evaluable for each specified time point. Here, IU/mL was abbreviated as "International units per milliliter".

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 29, 57, 85, and 113

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: IU/mL				
arithmetic mean (standard deviation)				
Day 29 (n= 4, 5)	-8.95 (± 14.19)	-1.40 (± 10.33)		
Day 57 (n= 4, 5)	9.68 (± 32.87)	2.46 (± 15.03)		
Day 85 (n= 4, 5)	-2.43 (± 7.57)	2.62 (± 23.77)		
Day 113 (n= 4, 4)	5.75 (± 26.71)	5.40 (± 5.42)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics - Change From Baseline in Pediatric Quality of Life (PedsQL™) Generic Core Scales at Day 85

End point title	Pharmacodynamics - Change From Baseline in Pediatric Quality of Life (PedsQL™) Generic Core Scales at Day 85

End point description:

The child, adolescent and parent/legal guardian PedsQL™ (version 4.0) generic core scales was used to measure HRQOL. The response information was completed by the subject and by a parent/legal guardian individually. PedsQL consisted of 23 item questionnaire encompassing 4 core scale domains:

Physical Functioning (8 items); Emotional Functioning (5 items); Social Functioning (5 items); and School Functioning (5 items). Items were scored on a 5 point Likert-type response scale: 0=never a problem to 1=almost never a problem; 2=sometimes a problem; 3=often a problem; and 4=almost always a problem). Once scored, items were reverse scored and linearly transformed to a 0-100 scale (0=100, 1=75, 2=50, 3=25, 4=0), where higher scores indicated better HRQOL. Total Scale Score was the sum of all the items over the number of items answered on all the Scales. Analysis was performed on ITT population. Here, "n= number analysed" signifies those subjects who were evaluable for specified category.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Day 85

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Parent (n= 4, 5)	-3.80 (± 13.76)	-13.04 (± 11.32)		
Subjects (n= 5, 5)	-3.04 (± 1.42)	-3.04 (± 9.01)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Serious TEAEs

End point title	Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Serious TEAEs

End point description:

An adverse event (AE) was any untoward medical occurrence in a subject or clinical investigation subject administered a pharmaceutical (investigational) product and which does not necessarily to had a causal relationship with this treatment. A Serious adverse event (SAE) was any untoward medical occurrence that at any dose: resulted in death, was life-threatening, required in-patient hospitalisation/prolongation of existing hospitalisation, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, was another medically important condition. TEAEs were defined as AEs that started prior to first study drug dose and that worsened after and the AEs that started on or after first study drug dose. TEAEs: Serious and non-serious AEs. Analysis was performed safety population that included subjects who had received at least one dose of study drug and had at least one post-baseline safety assessment.

End point type	Secondary

End point timeframe:

From Screening visit (signature of informed consent) up to last dose of study drug + 30 days (i.e., up to Day 113)

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: Subjects				
Subjects with TEAEs	2	0		
Subjects with Serious TEAEs	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Significant Abnormalities in 12-lead Electrocardiogram (ECG) Measurement

End point title	Number of Subjects With Clinically Significant Abnormalities in 12-lead Electrocardiogram (ECG) Measurement

End point description:

ECG measurements were taken with the subjects in resting position for at least 10 minutes. The investigator determined whether abnormal assessment results were clinically significant or not. The number of subjects with abnormal ECG findings were reported. Baseline was defined as the last measurement before first intake of study treatment on Day 1. Analysis was performed safety population.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Day 85

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: Subjects				
Baseline: Abnormal, clinically significant	0	0		
Day 85: Abnormal, clinically significant	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Abnormal Clinical Chemistry Parameters

End point title	Number of Subjects With Abnormal Clinical Chemistry Parameters

End point description:

Fasting blood samples (collected after 10 hours fasting) were used to assess the following clinical chemistry parameters: creatinine, glomerular filtration rate, creatinine clearance, total proteins, albumin, electrolytes (sodium, potassium, chloride, calcium), uric acid, urea nitrogen, urea, creatine phosphokinase (CPK), AST, ALT, GGT, ALP, total and conjugated bilirubin, high sensitivity C-reactive protein, fasting plasma glucose, fasting insulin, HOMA-IR, fructosamine, C-peptide, free fatty acids, glycated hemoglobin A1c, cystatin C. Abnormal clinical chemistry values were classified based on reference range: lower limit of normality (LLN); normal (>= LLN and <= upper limit of normality

[ULN]); > ULN and <3 ULN; >=3 ULN and <5 ULN and >=5 ULN. Only that parameter for which at least one value of abnormality were reported and presented in this endpoint. Analysis was performed on safety population.

End point type	Secondary

End point timeframe:

At Day 85 (i.e., end of treatment)

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: Subjects				
Total proteins: >ULN and <3 ULN	1	1		
Albumin: >ULN and <3 ULN	1	0		
CPK: >ULN and <3 ULN	0	1		
AST: >ULN and <3 ULN	3	0		
ALT: >ULN and <3 ULN	3	4		
ALT: >=3 ULN and <5 ULN	1	0		
ALT: >=5 ULN	1	0		
GGT: >ULN and <3 ULN	2	2		
GGT: >=3 ULN and <5 ULN	1	0		
GGT: >=5 ULN	1	0		
ALP: >ULN and <3 ULN	1	0		
Total Bilirubin: >ULN and <3 ULN	0	1		
Conjugated Bilirubin: >ULN and <3 ULN	0	1		
C Reactive Protein: >ULN and <3 ULN	0	1		
Fasting plasma glucose: >ULN and <3 ULN	1	0		
Fasting insulin: >ULN and <3 ULN	3	5		
Fasting insulin: >=3 ULN and <5 ULN	2	0		
C-peptide: >ULN and <3 ULN	4	2		
Hemoglobin A1C: >ULN and <3 ULN	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Abnormal Hematology and Coagulation Parameters

End point title	Number of Subjects With Abnormal Hematology and Coagulation Parameters

End point description:

Fasting blood samples (collected after 10 hours fasting) were used to assess the following hematology and coagulation parameters: hemoglobin, hematocrit, red blood cells (RBC), white blood cells (WBC), neutrophils, eosinophils, basophils, lymphocytes, monocytes, platelets, prothrombin time (PT) and international normalized ratio (INR). Hematology and coagulation values were classified based on the reference range: LLN; normal (>= LLN and <= ULN); > ULN and <3 ULN; >=3 ULN and <5 ULN and >=5 ULN. Analysis was performed on safety population.

End point type	Secondary

End point timeframe:

At Day 85 (i.e., end of treatment)

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: Subjects				
Hemoglobin: >ULN and <3 ULN	0	0		
Hematocrit: >ULN and <3 ULN	0	0		
RBC: >ULN and <3 ULN	0	1		
WBC: >ULN and <3 ULN	0	0		
Neutrophils: >ULN and <3 ULN	0	0		
Eosinophils: >ULN and <3 ULN	0	0		
Basophils: >ULN and <3 ULN	0	0		
Lymphocytes: >ULN and <3 ULN	0	0		
Monocytes: >ULN and <3 ULN	0	0		
Platelets: >ULN and <3 ULN	0	0		
PT: >ULN and <3 ULN	0	0		
INR: >ULN and <3 ULN	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Abnormal Urinalysis Parameters

End point title	Number of Subjects With Abnormal Urinalysis Parameters

End point description:

Blood samples were collected to assess the following urinalysis parameters: alpha-1 macroglobulin, N-acetyl glucosamide, neutrophil gelatinase-associated lipocalin (NGL), albumin, and creatinine. Abnormal urinalysis values were classified based on the reference range: LLN; normal (>= LLN and <= ULN); > ULN and <3 ULN; >=3 ULN and <5 ULN and >=5 ULN. Analysis was performed on safety population.

End point type	Secondary

End point timeframe:

At Day 85 (i.e., end of treatment)

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: Subjects				
Alpha-1 Microglobulin: >ULN and <3 ULN	0	0		
N-Acetyl Glucosamide: >ULN and <3 ULN	0	0		
NGL: >ULN and <3 ULN	0	0		

Albumin: : >ULN and <3 ULN	0	0		
Creatinine	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Abnormal Vital Signs

End point title	Number of Subjects With Abnormal Vital Signs

End point description:

Vital signs were taken before any invasive procedures. Following vital signs were assessed: systolic blood pressure, diastolic blood pressure, and heart rate. Abnormal vita signs was defined as any abnormal findings in the vital sign parameters and were categorised as 'abnormal, not clinically significant (NCS)' and 'abnormal, clinically significant (CS)'. Analysis was performed on safety population.

End point type	Secondary

End point timeframe:

At Day 85 (i.e., end of treatment)

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: Subjects				
Systolic Blood Pressure: Abnormal, NCS	0	0		
Systolic Blood Pressure: Abnormal, CS	0	0		
Diastolic Blood Pressure: Abnormal, NCS	0	0		
Diastolic Blood Pressure: Abnormal, CS	0	0		
Heart Rate: Abnormal, NCS	0	0		
Heart Rate: Abnormal, CS	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Significant Abnormalities in Physical Examination at Baseline, Days 15, 29, 57, 85 and 113

End point title	Number of Subjects With Clinically Significant Abnormalities in Physical Examination at Baseline, Days 15, 29, 57, 85 and 113

End point description:

Physical examination findings were collected according to pre-defined body systems: general appearance; skin; eyes; ears; nose; throat; neck and thyroid; lungs; heart; upper/lower extremities; lymph nodes; abdomen; musculoskeletal system; basic Neurological Assessment. Additional systems were evaluated as needed. Clinical significance was defined as any variation in assessment results that had medical relevance resulting in an alteration in medical care. Subjects with at least one clinically significant abnormality in physical examination were reported and presented in this endpoint. Baseline

was defined as the last measurement before first intake of study treatment on Day 1. Analysis was performed on safety population. Here, 'number of subjects analysed' signifies those subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 15, 29, 57, 85 and 113

End point values	Elafibranor 80 mg	Elafibranor 120mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	2		
Units: Subjects				
Baseline (Day 1)	4	2		
Day 15	0	0		
Day 29	1	0		
Day 57	0	0		
Day 85	0	0		
Day 113	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs were collected from screening through 30 days after last dose of study drug (i.e., up to Day 113) regardless of seriousness or relationship to study drug.

Adverse event reporting additional description:

Reported AEs were TEAEs that started prior to first study drug dose and that worsened after, and the AEs that started on or after first study drug dose. Analysis was performed on safety population.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Elafibranor 80 mg

Reporting group description:

Subjects received elafibranor 80 mg tablets orally once daily for 12 weeks.

Reporting group title	Elafibranor 120 mg

Reporting group description:

Subjects received elafibranor 120 mg tablets orally once daily for 12 weeks.

Serious adverse events	Elafibranor 80 mg	Elafibranor 120 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Elafibranor 80 mg	Elafibranor 120 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 5 (40.00%)	0 / 5 (0.00%)	
Hepatobiliary disorders			
Hepatomegaly			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Asthma			

subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 5 (0.00%) 0	
Infections and infestations Gastroenteritis viral subjects affected / exposed occurrences (all)	 1 / 5 (20.00%) 1	 0 / 5 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 April 2020	Protocol Amendment 3: The following changes were made to implement safeguards due to COVID-19 restrictions. - The screening window (i.e., the time from the signing of consent or the screening visit to randomisation) could had been extended up to 8 weeks if no on-site visit was possible earlier. . - Off-site study procedures could be performed in case a subject could not attend an on-site visit, including safety assessments via phone call, local laboratory assessments, delivery of the study drug to subjects, and visits to the subjects' homes. - The randomization visit (Visit 1) was excluded from the off-site options and needed to be completed on-site. - Safety and drug compliance procedures were updated to include the option of a phone call or, if safe and possible at the time, a direct visit to the subject.

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.

Due to lack of efficacy (but not due to safety) in Phase 3 trial of elafibranor in adult subjects with NASH and fibrosis, this study in pediatric NASH was prematurely terminated and therefore subjects >=12 to <=17 years of age were only involved.

Notes: