Clinical trial results:
A Multicenter, Double-Blind, Randomized, Placebo-Controlled, Phase 2 Study to Evaluate the Efficacy and Safety of Elafibranor at Doses of 80 mg and 120mg after 12 Weeks of Treatment in Patients With Primary Biliary Cholangitis (PBC) and Inadequate Response to Ursodeoxycholic Acid

Summary

EudraCT number	2016-003817-80
Trial protocol	ES GB FR
Global end of trial date	31 October 2018

Results information

Result version number	v1 (current)
This version publication date	28 August 2019
First version publication date	28 August 2019

Trial information

Trial identification

Sponsor protocol code	GFT505B-216-1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03124108
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Genfit SA
Sponsor organisation address	Parc Eurasante, avenue Eugene Avinee, France, 885
Public contact	Clinical Head, Genfit SA, clinicaltrial@genfit.com
Scientific contact	Clinical Head, Genfit SA, clinicaltrial@genfit.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	31 October 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 October 2018
Global end of trial reached?	Yes
Global end of trial date	31 October 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study was to evaluate the efficacy of elafibranor 80 milligram (mg) and 120 mg compared with placebo in subjects with primary biliary cholangitis (PBC) as measured by the relative change from baseline in serum alkaline phosphatase (ALP) levels.

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	05 April 2017
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	Spain: 6
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	United States: 23
Worldwide total number of subjects	45
EEA total number of subjects	22

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)	34
From 65 to 84 years	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 68 subjects were screened, out of which 45 subjects were randomized, 15 subjects in each of the 3 treatment groups.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Elafibranor 80mg

Arm description:

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

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

Dosage and administration details:

Subjects received elafibranor 80 milligram (mg) tablets 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	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

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

Arm title	Placebo

Arm description:

Subjects received matching placebo tablets orally once daily for 12 weeks.

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:
Subjects received placebo tablets orally once daily for 12 weeks.

Number of subjects in period 1	Elafibranor 80mg	Elafibranor 120mg	Placebo
Started	15	15	15
Completed	15	14	15
Not completed	0	1	0
Adverse event, non-fatal	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Elafibranor 80mg
Reporting group description:	
Subjects received elafibranor 80 milligram (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 title	Placebo
Reporting group description:	
Subjects received matching placebo tablets orally once daily for 12 weeks.	

Reporting group values	Elafibranor 80mg	Elafibranor 120mg	Placebo
Number of subjects	15	15	15
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	13	10	11
From 65-84 years	2	5	4
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	56.5	60.4	60.5
standard deviation	± 8.7	± 6.9	± 8.6
Gender categorical Units: Subjects			
Female	14	15	14
Male	1	0	1

Reporting group values	Total		
Number of subjects	45		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	34		

From 65-84 years	11		
85 years and over	0		

Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	43		
Male	2		

End points

End points reporting groups

Reporting group title	Elafibranor 80mg
Reporting group description:	
Subjects received elafibranor 80 milligram (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 title	Placebo
Reporting group description:	
Subjects received matching placebo tablets orally once daily for 12 weeks.	

Primary: Relative Change From Baseline in Serum Alkaline Phosphatase (ALP) Levels at Week 12 (Endpoint)

End point title	Relative Change From Baseline in Serum Alkaline Phosphatase (ALP) Levels at Week 12 (Endpoint)
End point description:	
Relative change from baseline is in serum ALP levels at Week 12 (endpoint) were reported. Relative change from baseline is defined as percentage (%) change from baseline to endpoint. The modified Intent-to-Treat (mITT) analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.	
End point type	Primary
End point timeframe:	
Baseline, Week 12 (Endpoint)	

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: Percent change				
arithmetic mean (standard deviation)	-48.264 (± 14.7676)	-40.640 (± 17.3624)	3.190 (± 14.8059)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Elafibranor 80mg
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in percentage
Point estimate	-52

Confidence interval	
level	95 %
sides	2-sided
lower limit	-62.5
upper limit	-41.5
Variability estimate	Standard error of the mean
Dispersion value	5.4

Statistical analysis title	Statistical Analysis 2
Comparison groups	Elafibranor 120mg v Placebo
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in percentage
Point estimate	-43.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-55.7
upper limit	-32.1
Variability estimate	Standard error of the mean
Dispersion value	6

Secondary: Percentage of subjects With Response Defined by Composite Risk Scores (ALP< 1.67 * Upper Limit of Normal [ULN] at Endpoint, Total Bilirubin [BIL] Within Normal Limits at Endpoint, and Greater Than [>] 15% ALP Reduction from Baseline to Endpoint)

End point title	Percentage of subjects With Response Defined by Composite Risk Scores (ALP< 1.67 * Upper Limit of Normal [ULN] at Endpoint, Total Bilirubin [BIL] Within Normal Limits at Endpoint, and Greater Than [>] 15% ALP Reduction from Baseline to Endpoint)

End point description:

Percentage of subjects with response defined by Composite Risk Scores (ALP Less than [<] 1.67 * ULN at endpoint, Total BIL within normal limits at endpoint, and > 15% ALP reduction from baseline to Endpoint) was reported. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

Up to Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: Percentage of subjects				
number (not applicable)	66.7	78.6	6.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects With Response Defined by Composite Risk Scores (ALP < 2 * Upper Limit of Normal at Endpoint, Total Bilirubin Within Normal Limits at Endpoint, and > 40% ALP Reduction from Baseline to Endpoint)

End point title	Percentage of subjects With Response Defined by Composite Risk Scores (ALP < 2 * Upper Limit of Normal at Endpoint, Total Bilirubin Within Normal Limits at Endpoint, and > 40% ALP Reduction from Baseline to Endpoint)

End point description:

Percentage of subjects with response defined by composite risk scores (ALP < 2 * ULN at endpoint, Total BIL within normal limits at endpoint, and > 40% ALP reduction from baseline to endpoint) was reported. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

Up to Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: Percentage of subjects				
number (not applicable)	73.3	42.9	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects With Response Based on PARIS I Risk Score at Endpoint

End point title	Percentage of subjects With Response Based on PARIS I Risk Score at Endpoint

End point description:

Percentage of subjects with response based on Paris I risk score was defined as ALP less than or equal to (<=) 3 * ULN and aspartate aminotransferase (AST) <= 2 * ULN and bilirubin within normal limits. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

At Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: Percentage of subjects				
number (not applicable)	80.0	78.6	53.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects With Response Based on PARIS II Risk Score at Endpoint

End point title	Percentage of subjects With Response Based on PARIS II Risk Score at Endpoint

End point description:

Percentage of subjects with response based on Paris II risk score was defined as ALP <= 1.5 * ULN and AST <= 1.5 * ULN and bilirubin within normal limits. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

At Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: Percentage of subjects				
number (not applicable)	53.3	50.0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects With Response Based on Toronto I Risk Score at Endpoint

End point title	Percentage of subjects With Response Based on Toronto I Risk Score at Endpoint

End point description:

Percentage of subjects with response based on Toronto I risk score was defined as ALP <= 1.67 *ULN. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

At Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: Percentage of subjects				
number (not applicable)	66.7	78.6	6.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects With Response Based on Toronto II Risk Score at Endpoint

End point title	Percentage of subjects With Response Based on Toronto II Risk Score at Endpoint

End point description:

Percentage of subjects with response based on Toronto II risk scores was defined as ALP <= 1.75 * ULN. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

At Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: Percentage of subjects				
number (not applicable)	66.7	78.6	6.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Median Percentage Risk as Assessed by United Kingdom-Primary Biliary

Cholangitis (UK-PBC) Risk Total Score at Endpoint

End point title	Median Percentage Risk as Assessed by United Kingdom-Primary Biliary Cholangitis (UK-PBC) Risk Total Score at Endpoint

End point description:

UK-PBC risk score at endpoint estimated that the median percentage risk that a subject treated with ursodeoxycholic acid (UDCA) will develop liver failure requiring liver transplant in 5, 10 and 15 years. UK-PBC score was calculated at each of the 3 survivor functions 1-baseline survival function^exp(0.0287854*[alpEPxuln-1.722136304] - 0.0422873*[{(altastEPxuln/10)^-1} - 8.675729006] + 1.4199 * [LN{bilEPxuln /10}+2.709607778] -1.960303*[albxlln-1.17673001]- 0.4161954*[pltxlln -1.873564875]). Where: Baseline survivor function=0. 982 (at 5 years); 0. 941 (at 10 years); 0.893 (at 15 years). alpEPxuln = ALP at endpoint/upper level normal ALP; altastEPxuln=(ALT, AST) at endpoint/ upper level normal of the value; bilEPxuln=bilirubin at endpoint/upper level normal bilirubin; albxlln=albumin at baseline/ albumin lower level normal; pltxlln=platelet count at baseline/ platelet count lower level normal. Population included mITT analysis

End point type	Secondary

End point timeframe:

At Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: Percentage risk				
median (full range (min-max))				
5 Years	0.80 (0.1 to 6.0)	0.95 (0.2 to 5.8)	1.30 (0.1 to 3.7)	
10 Years	2.60 (0.3 to 18.8)	3.05 (0.8 to 18.1)	4.40 (0.5 to 12.0)	
15 Years	4.70 (0.6 to 32.1)	5.55 (1.5 to 31.0)	8.00 (0.9 to 21.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects With Response Defined by 10, 20 and 40 Percent Reduction in Alkaline Phosphatase

End point title	Percentage of subjects With Response Defined by 10, 20 and 40 Percent Reduction in Alkaline Phosphatase

End point description:

Percentage of subjects with response (defined by at least 10%, 20%, and 40% decrease in ALP from baseline to Endpoint) reported. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

At Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: Percentage of subjects				
number (not applicable)				
10 Percent Reduction	93.3	92.9	13.3	
20 Percent Reduction	93.3	92.9	6.7	
40 Percent Reduction	86.7	57.1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects With Response Defined by Normalized Alkaline Phosphatase Levels at Endpoint

End point title	Percentage of subjects With Response Defined by Normalized Alkaline Phosphatase Levels at Endpoint

End point description:

The response was defined by normalized ALP levels (ALP ULN 105 units per liter [U/L] for females, 129 U/L for males) at endpoint.The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

At Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: Percentage of subjects				
number (not applicable)	13.3	21.4	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects With Response Defined by Normalized Bilirubin (BIL) at Endpoint

End point title	Percentage of subjects With Response Defined by Normalized Bilirubin (BIL) at Endpoint

End point description:

The response was defined by normalized BIL levels (BIL ULN <1.20 milligram per deciliter [mg/dL]) at endpoint.The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

At Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: Percentage of subjects				
number (not applicable)	86.7	92.9	93.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects With Response Defined by Normalized Albumin (ALB) Levels at Endpoint

End point title	Percentage of subjects With Response Defined by Normalized Albumin (ALB) Levels at Endpoint

End point description:

The response was defined by normalized ALB levels (3.5-5.2 gram per deciliter [g/dL] for ages 18-60 years; 3.2-4.6 g/ dL for ages 61-91 years) at endpoint. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

At Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: Percentage of subjects				
number (not applicable)	100	100	100	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Alanine Aminotransferase (ALT) Levels at Endpoint

End point title	Change From Baseline in Alanine Aminotransferase (ALT) Levels at Endpoint

End point description:

Change from baseline in ALT levels at endpoint was reported. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: U/L				
arithmetic mean (standard deviation)	-0.5 (± 57.38)	7.3 (± 29.13)	-1.2 (± 8.57)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Aspartate Aminotransferase (AST) Levels at Endpoint

End point title	Change From Baseline in Aspartate Aminotransferase (AST) Levels at Endpoint

End point description:

Change from baseline in AST levels at endpoint was reported. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: U/L				
arithmetic mean (standard deviation)	6.0 (± 55.29)	11.1 (± 27.96)	-4.3 (± 7.97)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Gamma-glutamyl Transferase (GGT) Levels at

Endpoint	
End point title	Change From Baseline in Gamma-glutamyl Transferase (GGT) Levels at Endpoint

End point description:

Change from baseline in GGT levels at endpoint was reported. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: U/L				
arithmetic mean (standard deviation)	-91.5 (± 95.30)	-61.9 (± 70.82)	0.6 (± 54.40)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in 5 Prime (') Nucleotidase Levels at Endpoint

End point title	Change From Baseline in 5 Prime (') Nucleotidase Levels at Endpoint

End point description:

Change from baseline in 5' nucleotidase levels at endpoint was reported. 5’ nucleotidase is an enzyme used as a biomarker of hepatobiliary cholestasis and is less sensitive but more specific than GGT and ALP. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: U/L				
arithmetic mean (standard deviation)	-7.81 (± 8.279)	-4.59 (± 13.067)	-0.47 (± 3.491)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Total Bilirubin (BIL) Levels at Endpoint

End point title	Change From Baseline in Total Bilirubin (BIL) Levels at Endpoint

End point description:

Change from baseline in total BIL levels at endpoint was reported. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: micromole per liter (mcmol/L)				
arithmetic mean (standard deviation)	-0.23 (± 3.425)	-0.51 (± 2.821)	-0.01 (± 3.548)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Conjugated Bilirubin Levels at Endpoint

End point title	Change From Baseline in Conjugated Bilirubin Levels at Endpoint

End point description:

Change from baseline in conjugated bilirubin levels at endpoint was reported. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: mcmol/L				
arithmetic mean (standard deviation)	0.34 (± 2.229)	-0.06 (± 0.596)	0.45 (± 1.526)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Albumin Levels at Endpoint

End point title	Change From Baseline in Albumin Levels at Endpoint

End point description:

Change from baseline in albumin levels at endpoint was reported. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: gram per liter (g/L)				
arithmetic mean (standard deviation)	2.2 (± 2.54)	2.3 (± 2.73)	0.0 (± 2.20)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Cholesterol Levels at Endpoint

End point title	Change From Baseline in Cholesterol Levels at Endpoint

End point description:

Change from baseline in cholesterol levels at endpoints was reported. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: millimole per liter (mmol/L)				
arithmetic mean (standard deviation)	-0.455 (± 0.7479)	-0.387 (± 0.6308)	0.043 (± 0.3706)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Low-density Lipoprotein (LDL) Cholesterol Levels at Endpoint

End point title	Change From Baseline in Low-density Lipoprotein (LDL) Cholesterol Levels at Endpoint

End point description:

Change from baseline in LDL-cholesterol at endpoint was reported. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: mmol/L				
arithmetic mean (standard deviation)	-0.366 (± 0.5919)	-0.334 (± 0.4848)	0.061 (± 0.3272)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in High-density Lipoprotein (HDL) Cholesterol Levels at Endpoint

End point title	Change From Baseline in High-density Lipoprotein (HDL) Cholesterol Levels at Endpoint

End point description:

Change from baseline in HDL-cholesterol levels at endpoint was reported. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: mmol/L				
arithmetic mean (standard deviation)	-0.017 (± 0.3898)	0.059 (± 0.3391)	-0.007 (± 0.2988)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Triglycerides Levels at Endpoint

End point title	Change From Baseline in Triglycerides Levels at Endpoint

End point description:

Change from baseline in triglycerides levels at endpoint was reported. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: mmol/L				
arithmetic mean (standard deviation)	-0.155 (± 0.3460)	-0.253 (± 0.2085)	-0.019 (± 0.3776)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Total Free Bile Acid Levels at Endpoint

End point title	Change From Baseline in Total Free Bile Acid Levels at Endpoint

End point description:

Change from baseline in total free bile acid levels at endpoint was reported. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: 10^-9 mole per liter (mol/L)				
arithmetic mean (standard deviation)	-248.88 (± 2496.672)	-673.71 (± 2962.097)	-135.20 (± 6777.727)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Total Conjugated Bile Acid Levels at Endpoint

End point title	Change From Baseline in Total Conjugated Bile Acid Levels at Endpoint

End point description:

Change from baseline in total conjugated bile acid levels at endpoint was reported. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: 10^-9 mol/L				
arithmetic mean (standard deviation)	5008.99 (± 17844.304)	-3280.16 (± 10941.769)	1873.22 (± 21795.349)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Total Bile Acid Levels at Endpoint

End point title	Change From Baseline in Total Bile Acid Levels at Endpoint

End point description:

Change from baseline in total bile acid levels at endpoint was reported. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: 10^-9 mol/L				
arithmetic mean (standard deviation)	4760.11 (± 18919.661)	-3953.86 (± 12008.620)	1738.02 (± 26521.746)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in 7 Alpha-hydroxy-4-cholesten-3-one Levels at Endpoint

End point title	Change From Baseline in 7 Alpha-hydroxy-4-cholesten-3-one Levels at Endpoint

End point description:

Change from baseline in 7 alpha-hydroxy-4-cholesten-3-one levels at endpoint was reported. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: 10^-9 mol/L				
arithmetic mean (standard deviation)	-16.29 (± 27.584)	-10.04 (± 28.606)	5.22 (± 10.848)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Fibroblast Growth Factor-19 Levels at Endpoint

End point title	Change From Baseline in Fibroblast Growth Factor-19 Levels at Endpoint

End point description:

Change from baseline in fibroblast growth factor-19 levels at endpoint was reported. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: nanogram per liter (ng/L)				
arithmetic mean (standard deviation)	-21.67 (± 52.588)	-16.96 (± 38.933)	-47.08 (± 69.560)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Immunoglobulin M (IgM) Levels at Endpoint

End point title	Change From Baseline in Immunoglobulin M (IgM) Levels at Endpoint

End point description:

Change from baseline in IgM levels at endpoint was reported. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: g/L				
arithmetic mean (standard deviation)	-0.339 (± 0.5846)	-0.472 (± 0.5507)	-0.076 (± 0.7227)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Tumor Necrosis Factor Levels at Endpoint

End point title	Change From Baseline in Tumor Necrosis Factor Levels at Endpoint

End point description:

Change from baseline in tumor necrosis factor levels at endpoint was reported. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: ng/L				
arithmetic mean (standard deviation)	0.066 (± 0.7829)	0.154 (± 1.1374)	0.053 (± 0.8329)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Transforming Growth Factor Beta Levels at Endpoint

End point title	Change From Baseline in Transforming Growth Factor Beta Levels at Endpoint

End point description:

Change from baseline in transforming growth factor beta levels at endpoint was reported. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: ng/L				
arithmetic mean (standard deviation)	734.7 (± 2103.75)	297.2 (± 2762.61)	-1163.0 (± 4295.49)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Interleukin 6 Levels at Endpoint

End point title	Change From Baseline in Interleukin 6 Levels at Endpoint

End point description:

Change from baseline in interleukin 6 levels at endpoint was reported. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: ng/L				
arithmetic mean (standard deviation)	-0.021 (± 0.8337)	-0.261 (± 0.5213)	-0.165 (± 0.5624)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Plasminogen Activator Inhibitor-1 Antigen (AG) Levels at Endpoint

End point title	Change From Baseline in Plasminogen Activator Inhibitor-1 Antigen (AG) Levels at Endpoint

End point description:

Change from baseline in plasminogen activator inhibitor-1 AG levels at endpoint was reported. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: microgram per liter (mcg/L)				
arithmetic mean (standard deviation)	-0.483 (± 2.9839)	-1.739 (± 4.6587)	-1.456 (± 4.6448)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Cytokeratin-18 Levels at Endpoint

End point title	Change From Baseline in Cytokeratin-18 Levels at Endpoint

End point description:

Change from baseline in cytokeratin-18 (M30 and M65) levels at endpoint was reported. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: picomole per liter (pmol/L)				
arithmetic mean (standard deviation)				
Cytokeratin-18 M30	26.12 (± 472.247)	163.33 (± 499.500)	17.93 (± 307.531)	
Cytokeratin-18 M65	114.31 (± 627.068)	238.97 (± 611.520)	-53.16 (± 131.934)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Autotaxin Levels at Endpoint

End point title	Change From Baseline in Autotaxin Levels at Endpoint

End point description:

Change from baseline in autotaxin levels at endpoint was reported. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: mcg/L				
arithmetic mean (standard deviation)	4.6 (± 156.92)	49.9 (± 77.25)	35.1 (± 161.58)	

Statistical analyses

No statistical analyses for this end point

Secondary: C-reactive Protein Level at Endpoint

End point title	C-reactive Protein Level at Endpoint

End point description:

C-reactive protein level at endpoint was reported. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: milligram per liter (mg/L)				
geometric mean (confidence interval 95%)	2.74 (1.81 to 4.14)	2.84 (1.68 to 4.78)	4.01 (2.52 to 6.37)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Haptoglobin Levels at Endpoint

End point title	Change From Baseline in Haptoglobin Levels at Endpoint

End point description:

Change from baseline in haptoglobin levels at endpoint was reported. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: g/L				
arithmetic mean (standard deviation)	-0.265 (± 0.4271)	-0.254 (± 0.1088)	0.025 (± 0.2244)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Fibrinogen Levels at Endpoint

End point title	Change From Baseline in Fibrinogen Levels at Endpoint

End point description:

Change from baseline in fibrinogen levels at endpoint was reported. The mITT analysis set included all randomized subjects who received at least one study drug dose with available baseline value and at least one post baseline value for the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: g/L				
arithmetic mean (standard deviation)	-0.865 (± 0.9472)	-0.452 (± 0.5780)	-0.072 (± 1.0936)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in 5D Itch Scale Total Score

End point title	Change From Baseline in 5D Itch Scale Total Score

End point description:

5D-Itch Scale is reliable, multidimensional measure of itching that has been validated in subjects with chronic pruritus to detect changes over time. It consists of 5 domains: duration, degree, direction, disability, and distribution. Duration, degree and direction domains each include 1 item, while disability domain has 4 items (sleep, leisure/social, housework/errands, work/school). All items of first 4 domains were measured on a 5-point Likert scale. Distribution domain included 16 potential locations of itch, 15 body part items (head/scalp, soles, face, palms, chest, abdomen, back, buttocks, thighs, lower legs,

tops of feet/toes, tops of hands/fingers, upper arms, groin, forearms) and 1 point of contact with clothing/bandages. Scores of each of 5 domains are achieved separately and then summed together to obtain total 5-D score. 5-D scores can range between 5 (no pruritus) and 25 (most severe pruritus). mITT population included. N= number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	12	15	
Units: Units on a scale				
arithmetic mean (standard deviation)	-2.1 (± 5.15)	-0.1 (± 2.19)	0.8 (± 4.93)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Pruritus as Assessed by Visual Analogue Scale (VAS) Total Score

End point title	Change From Baseline in Pruritus as Assessed by Visual Analogue Scale (VAS) Total Score

End point description:

The VAS is a reliable and validated method of pruritus assessment. The VAS is adequate in assessing the severity of the symptom; it does not take into account other aspects of pruritus, such as the relative impact of pruritus on quality of life. The VAS, for pruritus assessment, requires the subject to use abstract thought processes to convert their itch severity to a mark on a continuum. A subject draws a line anywhere on the scale ranging from 0 to 10 (where 0 represents 'no itching' and 10 represents 'worst possible itching') that best represents the severity of subject's itching and the scoring involves manual measuring of the mark with a ruler on range of 0 to 100 millimeter (mm). Higher scores indicate worse itching. mITT: randomized subjects received at least one study drug dose with available baseline value and at least one post baseline value for primary endpoint. Here 'N' (number of subjects analyzed) signifies subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	14	15	
Units: Units on a scale				
arithmetic mean (standard deviation)	-4.4 (± 22.80)	-4.7 (± 11.81)	9.3 (± 35.93)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Primary Biliary Cholangitis -40 (PBC-40) Quality of Life Questionnaire Scores

End point title	Change From Baseline in Primary Biliary Cholangitis -40 (PBC-40) Quality of Life Questionnaire Scores

End point description:

PBC-40 QoL Questionnaire is patient-derived, disease-specific QoL measure developed and validated for use in PBC. It consists of 9 domains with total 40 questions: 1) digestion and diet (questions 1-3, with total score of 15); 2) experiences (questions 4-7, with total score of 20); 3) itching (questions 8-10, with total score of 15); 4) fatigue (questions 11-18, with total score of 40); 5) effort and planning (questions 19-21, with total score of 15); 6) memory and concentration (questions 22-27, with total score of 30); 7) affects you as person (questions 28-33, with total score of 30); 8) affects your social life (questions 34-37, with total score of 20); 9) overall impact on your life (questions 38-40, with total score of 15). PBC-40 QoL Questionnaire has 40 questions, each scored on scale of 1-5 (1=least impact, 5=greatest impact). For each domain, scoring involved summing individual question response scores. Higher scores indicate poorer quality of life. mITT population included.

End point type	Secondary

End point timeframe:

Baseline, Week 12 (Endpoint)

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: Units on a scale				
arithmetic mean (standard deviation)				
Digestion and Diet	-0.3 (± 2.74)	-0.6 (± 2.24)	-0.6 (± 3.00)	
Experiences	0.6 (± 2.64)	-1.3 (± 1.77)	-0.7 (± 3.69)	
Itching	-0.9 (± 6.19)	-4.1 (± 6.56)	2.1 (± 5.78)	
Fatigue	-1.9 (± 4.10)	-1.4 (± 2.71)	-1.5 (± 5.04)	
Effort and Planning	-0.9 (± 2.03)	-0.8 (± 1.31)	-0.9 (± 1.98)	
Memory and concentration	0.1 (± 3.26)	-1.5 (± 3.33)	-0.5 (± 3.25)	
Affecting you as a Person	-1.8 (± 3.78)	-2.5 (± 2.85)	-1.3 (± 3.22)	
Effects on your Social Life	1.3 (± 3.08)	0.0 (± 1.47)	1.4 (± 4.79)	
Impact on your Life	-0.1 (± 3.04)	0.6 (± 0.63)	-1.0 (± 3.30)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects With Treatment Emergent Adverse Events (TEAEs) and Serious Treatment Emergent Adverse

End point title	Number of subjects With Treatment Emergent Adverse Events (TEAEs) and Serious Treatment Emergent Adverse

End point description:

An adverse event (AE) is defined as any untoward medical occurrence in patient or clinical investigation patient administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. A serious adverse event (SAE) is any untoward medical occurrence that

at any dose: results in death, is life-threatening, requires inpatient hospitalization/prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is congenital anomaly/birth defect, is another medically important condition. TEAEs is defined as it is not present when active phase of study begins and is not a chronic condition that is part of patient's medical history, or it is present at start of active phase or as part of patient's medical history, but severity/frequency increases during active phase. Safety Set included all randomized subjects who were administered at least one dose.

End point type	Secondary

End point timeframe:

Up To Week 12

End point values	Elafibranor 80mg	Elafibranor 120mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	15	
Units: subjects				
number (not applicable)				
TEAEs	12	13	12	
Serious TEAEs	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to 16 Weeks	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0
Reporting groups	
Reporting group title	Elafibranor 80mg
Reporting group description: subjects received elafibranor 80 milligram (mg) tablets orally once daily for 12 weeks.	
Reporting group title	Placebo
Reporting group description: subjects received matching placebo 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.	

Serious adverse events	Elafibranor 80mg	Placebo	Elafibranor 120mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	2 / 15 (13.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Post procedural stroke			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ischaemic Stroke			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Autoimmune Hepatitis			

subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Elafibranor 80mg	Placebo	Elafibranor 120mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 15 (80.00%)	12 / 15 (80.00%)	13 / 15 (86.67%)
Surgical and medical procedures			
Stent Removal			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	3 / 15 (20.00%)
occurrences (all)	1	0	3
Influenza Like Illness			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Local Swelling			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Peripheral Swelling			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			

Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Cough			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Sleep Disorder			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Investigations			
Blood Bilirubin Increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Blood Cholesterol Increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Blood Urine Present			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Cystoscopy			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram Abnormal			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Gammaglutamylctransferase Increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Liver Palpable			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Transaminases Increased			

subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Urine Albumin/Creatinine Ratio Increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2
Urobilinogen Urine Increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
White Blood Cells Urine			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Post-traumatic Neck Syndrome			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Cerebral Amyloid Angiopathy			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	2 / 15 (13.33%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	2	1	0
Dysgeusia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	2 / 15 (13.33%)	1 / 15 (6.67%)	2 / 15 (13.33%)
occurrences (all)	3	1	2
Lumbar Radiculopathy			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Eye disorders			
Dry Eye			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Eye ulcer			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Scleral haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Abdominal Pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Abdominal Pain Upper			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Constipation			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Diarrhoea			
subjects affected / exposed	0 / 15 (0.00%)	2 / 15 (13.33%)	2 / 15 (13.33%)
occurrences (all)	0	2	2
Dry Mouth			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Nausea			

subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	3 / 15 (20.00%)
occurrences (all)	0	1	3
Rectal Haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Photosensitivity Reaction			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	3 / 15 (20.00%)	2 / 15 (13.33%)	3 / 15 (20.00%)
occurrences (all)	3	3	3
Skin Disorder			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Albuminuria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	3
Chromaturia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Nephrolithiasis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Nitrituria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Polyuria			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Proteinuria			

subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2
Renal colic			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Renal Pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Bone Pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Pain in Extremity			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Escherichia Urinary Tract Infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Gastroenteritis Viral			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Labyrinthitis			

subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Otitis Externa			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Urinary Tract Infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	3 / 15 (20.00%)
occurrences (all)	1	0	3
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	3 / 15 (20.00%)	2 / 15 (13.33%)	0 / 15 (0.00%)
occurrences (all)	3	2	0
Vulvovaginal Candidiasis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 December 2017	The overall reason for this amendment was to include an end of study (EOS) visit for all subjects who completed the double-blind treatment period (at least 16 days but not more than 30 days after visit 5 [Week 12]), to clarify instructions for investigators and to add windows for pharmacokinetic (PK) sample collection.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported