



## 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              |
| <b>Arm title</b>             | 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.

|                  |                   |
|------------------|-------------------|
| <b>Arm title</b> | 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.

|                  |         |
|------------------|---------|
| <b>Arm title</b> | 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 |

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**Dosage and administration details:**

Subjects received placebo tablets orally once daily for 12 weeks.

| <b>Number of subjects in period 1</b> | 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<br>Units: years<br>arithmetic mean<br>standard deviation | -  |  |  |
| Gender categorical<br>Units: Subjects                                   |    |  |  |
| Female  | 43 |  |  |
| Male  | 2  |  |  |

## End points

### End points reporting groups

|   |                   |
|---|-------------------|
| Reporting group title   | Elafibranor 80mg  |
| Reporting group description:<br>Subjects received elafibranor 80 milligram (mg) tablets orally once daily for 12 weeks. |                   |
| Reporting group title   | Elafibranor 120mg |
| Reporting group description:<br>Subjects received elafibranor 120 mg tablets orally once daily for 12 weeks.            |                   |
| Reporting group title   | Placebo           |
| Reporting group description:<br>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:<br>Relative change from baseline 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:<br>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                        |

|   |                             |
|---|-----------------------------|
| <b>Statistical analysis title</b>       | 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<br>80mg | Elafibranor<br>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<br>80mg | Elafibranor<br>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 ( $\leq$ ) 3 \* ULN and aspartate aminotransferase (AST)  $\leq$  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<br>80mg | Elafibranor<br>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  $\leq 1.5 \times$  ULN and AST  $\leq 1.5 \times$  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<br>80mg | Elafibranor<br>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  $ALP \leq 1.67 \times ULN$ . 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<br>80mg | Elafibranor<br>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  $ALP \leq 1.75 \times ULN$ . 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<br>80mg | Elafibranor<br>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:<br>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 $\exp(0.0287854 * [\text{alpEPxuln} - 1.722136304] - 0.0422873 * \{(\text{altastEPxuln}/10)^{-1} - 8.675729006\} + 1.4199 * [\text{LN}\{\text{bilEPxuln}/10\} + 2.709607778] - 1.960303 * [\text{albxlln} - 1.17673001] - 0.4161954 * [\text{pltxlln} - 1.873564875])$ . 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:<br>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:<br>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:<br>At Week 12 (Endpoint)  |   |

| End point values              | Elafibranor<br>80mg | Elafibranor<br>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:<br>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:<br>At Week 12 (Endpoint)   |  |

| End point values              | Elafibranor<br>80mg | Elafibranor<br>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:<br>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<br>80mg | Elafibranor<br>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<br>80mg | Elafibranor<br>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<br>80mg | Elafibranor<br>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<br>80mg | Elafibranor<br>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<br>80mg | Elafibranor<br>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 (±<br>95.30)  | -61.9 (±<br>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<br>80mg | Elafibranor<br>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 (±<br>8.279)  | -4.59 (±<br>13.067)  | -0.47 (±<br>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<br>80mg     | Elafibranor<br>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 ( $\pm$<br>3.425) | -0.51 ( $\pm$<br>2.821) | -0.01 ( $\pm$<br>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<br>80mg | Elafibranor<br>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 ( $\pm$ 2.229) | -0.06 ( $\pm$<br>0.596) | 0.45 ( $\pm$ 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<br>80mg | Elafibranor<br>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<br>80mg  | Elafibranor<br>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 (±<br>0.7479) | -0.387 (±<br>0.6308) | 0.043 (±<br>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<br>80mg  | Elafibranor<br>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 (±<br>0.5919) | -0.334 (±<br>0.4848) | 0.061 (±<br>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<br>80mg       | Elafibranor<br>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 ( $\pm$<br>0.3898) | 0.059 ( $\pm$<br>0.3391) | -0.007 ( $\pm$<br>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:<br>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:<br>Baseline, Week 12 (Endpoint)   |  |

| End point values                     | Elafibranor<br>80mg       | Elafibranor<br>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 ( $\pm$<br>0.3460) | -0.253 ( $\pm$<br>0.2085) | -0.019 ( $\pm$<br>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:<br>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<br>80mg     | Elafibranor<br>120mg    | Placebo                 |  |
|--|-------------------------|-------------------------|-------------------------|--|
| Subject group type                             | Reporting group         | Reporting group         | Reporting group         |  |
| Number of subjects analysed                    | 15                      | 14                      | 15                      |  |
| Units: 10 <sup>-9</sup> mole per liter (mol/L) |                         |                         |                         |  |
| arithmetic mean (standard deviation)           | -248.88 (±<br>2496.672) | -673.71 (±<br>2962.097) | -135.20 (±<br>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<br>80mg      | Elafibranor<br>120mg      | Placebo                  |  |
|--------------------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type                   | Reporting group          | Reporting group           | Reporting group          |  |
| Number of subjects analysed          | 15                       | 14                        | 15                       |  |
| Units: 10 <sup>-9</sup> mol/L        |                          |                           |                          |  |
| arithmetic mean (standard deviation) | 5008.99 (±<br>17844.304) | -3280.16 (±<br>10941.769) | 1873.22 (±<br>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<br>80mg      | Elafibranor<br>120mg      | Placebo                  |  |
|--------------------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type                   | Reporting group          | Reporting group           | Reporting group          |  |
| Number of subjects analysed          | 15                       | 14                        | 15                       |  |
| Units: 10 <sup>-9</sup> mol/L        |                          |                           |                          |  |
| arithmetic mean (standard deviation) | 4760.11 (±<br>18919.661) | -3953.86 (±<br>12008.620) | 1738.02 (±<br>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<br>80mg  | Elafibranor<br>120mg | Placebo            |  |
|--------------------------------------|----------------------|----------------------|--------------------|--|
| Subject group type                   | Reporting group      | Reporting group      | Reporting group    |  |
| Number of subjects analysed          | 15                   | 14                   | 15                 |  |
| Units: 10 <sup>-9</sup> mol/L        |                      |                      |                    |  |
| arithmetic mean (standard deviation) | -16.29 (±<br>27.584) | -10.04 (±<br>28.606) | 5.22 (±<br>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<br>80mg       | Elafibranor<br>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 ( $\pm$<br>52.588) | -16.96 ( $\pm$<br>38.933) | -47.08 ( $\pm$<br>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<br>80mg       | Elafibranor<br>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 ( $\pm$<br>0.5846) | -0.472 ( $\pm$<br>0.5507) | -0.076 ( $\pm$<br>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:<br>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:<br>Baseline, Week 12 (Endpoint)   |  |

| End point values                     | Elafibranor<br>80mg | Elafibranor<br>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 (±<br>0.7829) | 0.154 (±<br>1.1374)  | 0.053 (±<br>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:<br>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:<br>Baseline, Week 12 (Endpoint)   |  |

| End point values                     | Elafibranor<br>80mg  | Elafibranor<br>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 (±<br>2103.75) | 297.2 (±<br>2762.61) | -1163.0 (±<br>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<br>80mg       | Elafibranor<br>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 ( $\pm$<br>0.8337) | -0.261 ( $\pm$<br>0.5213) | -0.165 ( $\pm$<br>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<br>80mg       | Elafibranor<br>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 ( $\pm$<br>2.9839) | -1.739 ( $\pm$<br>4.6587) | -1.456 ( $\pm$<br>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<br>80mg   | Elafibranor<br>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 (±<br>472.247)  | 163.33 (±<br>499.500) | 17.93 (±<br>307.531)  |  |
| Cytokeratin-18 M65                   | 114.31 (±<br>627.068) | 238.97 (±<br>611.520) | -53.16 (±<br>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<br>80mg | Elafibranor<br>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<br>80mg | Elafibranor<br>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<br>80mg  | Elafibranor<br>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 (±<br>0.4271) | -0.254 (±<br>0.1088) | 0.025 (±<br>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:<br>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:<br>Baseline, Week 12 (Endpoint)  |   |

| End point values                     | Elafibranor<br>80mg  | Elafibranor<br>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 (±<br>0.9472) | -0.452 (±<br>0.5780) | -0.072 (±<br>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:<br>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<br>80mg | Elafibranor<br>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<br>80mg | Elafibranor<br>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 %

| <b>Non-serious adverse events</b>                     | 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              |
| Gammaglutamyltransferase 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<br>subjects affected / exposed<br>occurrences (all)              | 1 / 15 (6.67%)<br>2 | 0 / 15 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Eye disorders  |                     |                      |                      |
| Dry Eye<br>subjects affected / exposed<br>occurrences (all)              | 0 / 15 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |
| Eye ulcer<br>subjects affected / exposed<br>occurrences (all)            | 0 / 15 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |
| Scleral haemorrhage<br>subjects affected / exposed<br>occurrences (all)  | 0 / 15 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |
| Gastrointestinal disorders   |                     |                      |                      |
| Abdominal distension<br>subjects affected / exposed<br>occurrences (all) | 0 / 15 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1  | 0 / 15 (0.00%)<br>0  |
| Abdominal Pain<br>subjects affected / exposed<br>occurrences (all)       | 1 / 15 (6.67%)<br>1 | 0 / 15 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |
| Abdominal Pain Upper<br>subjects affected / exposed<br>occurrences (all) | 0 / 15 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1  | 1 / 15 (6.67%)<br>1  |
| Constipation<br>subjects affected / exposed<br>occurrences (all)         | 0 / 15 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1  | 1 / 15 (6.67%)<br>1  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)            | 0 / 15 (0.00%)<br>0 | 2 / 15 (13.33%)<br>2 | 2 / 15 (13.33%)<br>2 |
| Dry Mouth<br>subjects affected / exposed<br>occurrences (all)            | 0 / 15 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |
| Dyspepsia<br>subjects affected / exposed<br>occurrences (all)            | 0 / 15 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1  | 0 / 15 (0.00%)<br>0  |
| Nausea   |                     |                      |                      |

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

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported