# Clinical trial results:
# A Phase 2, Randomized, Double-Blind, Placebo Controlled Study Evaluating the Safety, Tolerability, and Efficacy of GS-9674 in Subjects with Primary Biliary Cholangitis Without Cirrhosis

## Summary

| | |
|---|---|
| EudraCT number | 2016-002443-42 |
| Trial protocol | GB AT |
| Global end of trial date | 04 September 2019 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 19 September 2020 |
| First version publication date | 19 September 2020 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | GS-US-427-4024 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02943447 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Gilead Sciences |
| Sponsor organisation address | 333 Lakeside Drive, Foster City, CA, United States, 94404 |
| Public contact | Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com |
| Scientific contact | Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.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 | 04 September 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 04 September 2019 |
| Global end of trial reached? | Yes |
| Global end of trial date | 04 September 2019 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the safety and tolerability of cilofexor in adults with primary biliary cholangitis
(PBC).

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 01 December 2016 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | United States: 35 |
| Country: Number of subjects enrolled | Canada: 21 |
| Country: Number of subjects enrolled | United Kingdom: 8 |
| Country: Number of subjects enrolled | Austria: 7 |
| Worldwide total number of subjects | 71 |
| EEA total number of subjects | 15 |

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) | 63 |
| From 65 to 84 years | 8 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Participants were enrolled at study sites in United States, Canada, United Kingdom, and Austria. The first participant was screened on 01 December 2016. The last study visit occurred on 4 September 2019.

### Pre-assignment

Screening details:

130 participants were screened.

### Period 1

| | |
|---|---|
| Period 1 title | Blinded Study Phase |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Blinded Study Phase: Cilofexor 100 mg |

Arm description:

Cilofexor 100 mg tablet + placebo to match cilofexor 30 mg tablet orally once daily for 12 weeks.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Cilofexor |
| Investigational medicinal product code | |
| Other name | GS-9674 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

100 mg tablet administered orally once daily, with food

| | |
|---|---|
| Investigational medicinal product name | Placebo to match cilofexor 30 mg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Tablet(s) administered orally once daily, with food

| | |
|---|---|
| **Arm title** | Blinded Study Phase: Cilofexor 30 mg |

Arm description:

Cilofexor 30 mg tablet + placebo to match cilofexor 100 mg tablet orally once daily for 12 weeks.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Cilofexor |
| Investigational medicinal product code | |
| Other name | GS-9674 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

30 mg tablet administered orally once daily, with food

| | |
|---|---|
| Investigational medicinal product name | Placebo to match cilofexor 100 mg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Tablet(s) administered orally once daily, with food

| **Arm title** | Blinded Study Phase: Placebo |
|---|---|

Arm description:

Placebo to match cilofexor 100 mg tablet + placebo to match cilofexor 30 mg tablet orally once daily for 12 weeks.

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo to match cilofexor 100 mg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Tablet(s) administered orally once daily, with food

| | |
|---|---|
| Investigational medicinal product name | Placebo to match cilofexor 30 mg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Tablet(s) administered orally once daily, with food

| **Number of subjects in period 1** | Blinded Study Phase: Cilofexor 100 mg | Blinded Study Phase: Cilofexor 30 mg | Blinded Study Phase: Placebo |
|---|---|---|---|
| Started | 28 | 30 | 13 |
| Completed | 23 | 28 | 12 |
| Not completed | 5 | 2 | 1 |
| Adverse event | 3 | - | - |
| Investigator`s discretion | 1 | - | - |
| Withdrew consent | 1 | 2 | 1 |

## Period 2

| | |
|---|---|
| Period 2 title | Open-Label Extension Phase |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |

| **Arm title** | OLE Phase: From Cilofexor 100 mg |
|---|---|

Arm description:

Following Blinded Study Phase, participants in the Cilofexor 100 mg group, willing to enter Open-Label Extension (OLE) Phase received open-label cilofexor 100 mg tablet orally once daily for 97.4 weeks.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Cilofexor 100 mg |
| Investigational medicinal product code | |
| Other name | GS-9674 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Tablet(s) administered orally once daily, with food

| **Arm title** | OLE Phase: From Cilofexor 30 mg |
|---|---|

Arm description:

Following Blinded Study Phase, participants in the Cilofexor 30 mg group, willing to enter OLE Phase received open-label cilofexor 100 mg tablet orally once daily for 96.1 weeks.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Cilofexor 100 mg |
| Investigational medicinal product code | |
| Other name | GS-9674 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Tablet(s) administered orally once daily, with food

| **Arm title** | OLE Phase: From Placebo |
|---|---|

Arm description:

Following Blinded Study Phase, participants in the Placebo group, willing to enter OLE Phase received open-label cilofexor 100 mg tablet orally once daily for 97.3 weeks.

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Cilofexor 100 mg |
| Investigational medicinal product code | |
| Other name | GS-9674 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Tablet(s) administered orally once daily, with food

| **Number of subjects in period 2** | OLE Phase: From Cilofexor 100 mg | OLE Phase: From Cilofexor 30 mg | OLE Phase: From Placebo |
|---|---|---|---|
| Started | 23 | 28 | 12 |
| Completed | 5 | 3 | 2 |
| Not completed | 18 | 25 | 10 |
| Study terminated by sponsor | 10 | 12 | 6 |
| Adverse event | 4 | 7 | 3 |
| Withdrew consent | 1 | 1 | 1 |
| Lost to follow-up | - | 1 | - |
| Lack of efficacy | 3 | 4 | - |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Blinded Study Phase: Cilofexor 100 mg |
| Reporting group description: | |
| Cilofexor 100 mg tablet + placebo to match cilofexor 30 mg tablet orally once daily for 12 weeks. | |
| Reporting group title | Blinded Study Phase: Cilofexor 30 mg |
| Reporting group description: | |
| Cilofexor 30 mg tablet + placebo to match cilofexor 100 mg tablet orally once daily for 12 weeks. | |
| Reporting group title | Blinded Study Phase: Placebo |
| Reporting group description: | |
| Placebo to match cilofexor 100 mg tablet + placebo to match cilofexor 30 mg tablet orally once daily for 12 weeks. | |

| Reporting group values | Blinded Study Phase: Cilofexor 100 mg | Blinded Study Phase: Cilofexor 30 mg | Blinded Study Phase: Placebo |
|---|---|---|---|
| Number of subjects | 28 | 30 | 13 |
| Age categorical | | | |
| Units: Subjects | | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 54 | 57 | 58 |
| standard deviation | ± 9.8 | ± 6.3 | ± 5.9 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 28 | 26 | 12 |
| Male | 0 | 4 | 1 |
| Race | | | |
| Not Permitted = local regulators did not allow collection of race information. | | | |
| Units: Subjects | | | |
| Asian | 2 | 0 | 0 |
| Black or African American | 0 | 1 | 0 |
| White | 26 | 27 | 13 |
| Not Permitted | 0 | 1 | 0 |
| Other | 0 | 1 | 0 |
| Ethnicity | | | |
| Not Permitted = local regulators did not allow collection of ethnicity information. | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 1 | 1 | 2 |
| Not Hispanic or Latino | 26 | 28 | 11 |
| Not Permitted | 1 | 1 | 0 |

| Reporting group values | Total | | |
|---|---|---|---|
| Number of subjects | 71 | | |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|---|---|---|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | -<br><br><br> | | |
| Gender categorical<br>Units: Subjects | | | |
| Female<br>Male | 66<br>5 | | |
| Race | | | |
| Not Permitted = local regulators did not allow collection of race information. | | | |
| Units: Subjects | | | |
| Asian<br>Black or African American<br>White<br>Not Permitted<br>Other | 2<br>1<br>66<br>1<br>1 | | |
| Ethnicity | | | |
| Not Permitted = local regulators did not allow collection of ethnicity information. | | | |
| Units: Subjects | | | |
| Hispanic or Latino<br>Not Hispanic or Latino<br>Not Permitted | 4<br>65<br>2 | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Blinded Study Phase: Cilofexor 100 mg |
| Reporting group description: | |
| Cilofexor 100 mg tablet + placebo to match cilofexor 30 mg tablet orally once daily for 12 weeks. | |
| Reporting group title | Blinded Study Phase: Cilofexor 30 mg |
| Reporting group description: | |
| Cilofexor 30 mg tablet + placebo to match cilofexor 100 mg tablet orally once daily for 12 weeks. | |
| Reporting group title | Blinded Study Phase: Placebo |
| Reporting group description: | |
| Placebo to match cilofexor 100 mg tablet + placebo to match cilofexor 30 mg tablet orally once daily for 12 weeks. | |
| Reporting group title | OLE Phase: From Cilofexor 100 mg |
| Reporting group description: | |
| Following Blinded Study Phase, participants in the Cilofexor 100 mg group, willing to enter Open-Label Extension (OLE) Phase received open-label cilofexor 100 mg tablet orally once daily for 97.4 weeks. | |
| Reporting group title | OLE Phase: From Cilofexor 30 mg |
| Reporting group description: | |
| Following Blinded Study Phase, participants in the Cilofexor 30 mg group, willing to enter OLE Phase received open-label cilofexor 100 mg tablet orally once daily for 96.1 weeks. | |
| Reporting group title | OLE Phase: From Placebo |
| Reporting group description: | |
| Following Blinded Study Phase, participants in the Placebo group, willing to enter OLE Phase received open-label cilofexor 100 mg tablet orally once daily for 97.3 weeks. | |

### Primary: Percentage of Participants Experiencing Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs) in the Blinded Study Phase

| | |
|---|---|
| End point title | Percentage of Participants Experiencing Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs) in the Blinded Study Phase[1] |
| End point description: | |
| The Safety Analysis Set included all participants who took at least 1 dose of study drug. | |
| End point type | Primary |
| End point timeframe: | |
| First dose date up to Week 12 + 30 days | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical comparison was planned or performed.

| End point values | Blinded Study Phase: Cilofexor 100 mg | Blinded Study Phase: Cilofexor 30 mg | Blinded Study Phase: Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 28 | 30 | 13 | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| TEAEs | 89.3 | 76.7 | 84.6 | |
| TESAEs | 0.0 | 3.3 | 0.0 | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Participants Experiencing TEAEs and TESAEs in the Open-Label Extension (OLE) Phase

| End point title | Percentage of Participants Experiencing TEAEs and TESAEs in the Open-Label Extension (OLE) Phase[2] |
|---|---|

End point description:

The OLE Analysis Set included all participants who took at least 1 dose of study drug in the OLE Phase.

| End point type | Primary |
|---|---|

End point timeframe:

First dose date in the OLE phase up to last dose date (Maximum: 97.4 weeks) + 30 days

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical comparison was planned or performed.

| End point values | OLE Phase: From Cilofexor 100 mg | OLE Phase: From Cilofexor 30 mg | OLE Phase: From Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 23 | 28 | 12 | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| TEAEs | 95.7 | 89.3 | 100.0 | |
| TESAEs | 4.3 | 0.0 | 0.0 | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Participants Who Experienced Graded Laboratory Abnormalities in the Blinded Study Phase

| End point title | Percentage of Participants Who Experienced Graded Laboratory Abnormalities in the Blinded Study Phase[3] |
|---|---|

End point description:

Treatment-emergent laboratory abnormalities were defined as values that increase at least one toxicity grade from baseline. The most severe graded abnormality from all tests was counted for each participant. Participants in the Safety Analysis Set were analyzed.

| End point type | Primary |
|---|---|

End point timeframe:

First dose date up to Week 12 + 30 days

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical comparison was planned or performed.

| End point values | Blinded Study Phase: Cilofexor 100 mg | Blinded Study Phase: Cilofexor 30 mg | Blinded Study Phase: Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 28 | 30 | 13 | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Any Graded Laboratory Abnormality | 85.7 | 86.7 | 92.3 | |
| Grade 4 or above Laboratory Abnormalities | 0.0 | 3.3 | 0.0 | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Participants Who Experienced Graded Laboratory Abnormalities in the OLE Phase

| End point title | Percentage of Participants Who Experienced Graded Laboratory Abnormalities in the OLE Phase[4] |
|---|---|

End point description:

Treatment-emergent laboratory abnormalities were defined as values that increase at least one toxicity grade from
baseline. The most severe graded abnormality from all tests was counted for each participant.
Participants in the OLE Analysis Set were analyzed.

| End point type | Primary |
|---|---|

End point timeframe:

First dose date in the OLE phase up to last dose date (Maximum: 97.4 weeks) + 30 days

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical comparison was planned or performed.

| End point values | OLE Phase: From Cilofexor 100 mg | OLE Phase: From Cilofexor 30 mg | OLE Phase: From Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 23 | 28 | 12 | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Any Graded Laboratory Abnormality | 91.3 | 96.4 | 100.0 | |
| Grade 4 or above Laboratory Abnormalities | 0.0 | 0.0 | 0.0 | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Blinded Study Phase: First dose date up to Week 12 + 30 days; Open-Label Extension (OLE) Phase: First dose date in the (OLE) Phase up to last dose date (Maximum: 97.4 weeks) + 30 days

Adverse event reporting additional description:

The Safety Analysis Set for Blinded Study phase included all participants who took at least 1 dose of study drug
in Blinded Study phase and the OLE Analysis Set included all participants who took at least 1 dose of study
drug in OLE phase.

| | |
|---|---|
| Assessment type | Systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 22.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Blinded Study Phase: Cilofexor 100 mg |

Reporting group description:

Blinded Study Phase: Cilofexor 100 mg tablet + placebo to match cilofexor 30 mg tablet orally once daily for 12 weeks.

| | |
|---|---|
| Reporting group title | Blinded Study Phase: Cilofexor 30 mg |

Reporting group description:

Blinded Study Phase: Cilofexor 30 mg tablet + placebo to match cilofexor 100 mg tablet orally once daily for 12 weeks.

| | |
|---|---|
| Reporting group title | Blinded Study Phase: Placebo |

Reporting group description:

Blinded Study Phase: Placebo to match cilofexor 100 mg tablet + placebo to match cilofexor 30 mg tablet orally once daily for 12 weeks.

| | |
|---|---|
| Reporting group title | OLE Phase: From Cilofexor 100 mg |

Reporting group description:

OLE Phase: Following Blinded Study Phase, participants in the Cilofexor 100 mg group, willing to enter OLE Phase received open-label cilofexor 100 mg tablet orally once daily for 97.4 weeks.

| | |
|---|---|
| Reporting group title | OLE Phase: From Cilofexor 30 mg |

Reporting group description:

OLE Phase: Following Blinded Study Phase, participants in the Cilofexor 30 mg group, willing to enter OLE Phase received open-label cilofexor 100 mg tablet orally once daily for 96.1 weeks.

| | |
|---|---|
| Reporting group title | OLE Phase: From Placebo |

Reporting group description:

OLE Phase: Following Blinded Study Phase, participants in the Placebo group, willing to enter OLE Phase received open-label cilofexor 100 mg tablet orally once daily for 97.3 weeks.

| Serious adverse events | Blinded Study Phase: Cilofexor 100 mg | Blinded Study Phase: Cilofexor 30 mg | Blinded Study Phase: Placebo |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 30 (3.33%) | 0 / 13 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Invasive ductal breast carcinoma | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 30 (3.33%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | OLE Phase: From Cilofexor 100 mg | OLE Phase: From Cilofexor 30 mg | OLE Phase: From Placebo |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 0 / 28 (0.00%) | 0 / 12 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Invasive ductal breast carcinoma | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 0 / 28 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 28 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| **Non-serious adverse events** | Blinded Study Phase: Cilofexor 100 mg | Blinded Study Phase: Cilofexor 30 mg | Blinded Study Phase: Placebo |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 21 / 28 (75.00%) | 18 / 30 (60.00%) | 11 / 13 (84.62%) |
| Vascular disorders | | | |
| Hypertension | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 30 (3.33%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Flushing | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 5 / 28 (17.86%) | 2 / 30 (6.67%) | 3 / 13 (23.08%) |
| occurrences (all) | 5 | 2 | 3 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 30 (3.33%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 1 | 1 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cyst | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Suprapubic pain | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immune system disorders | | | |
| Seasonal allergy | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 30 (3.33%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Psychiatric disorders | | | |

| | | | |
|---|---|---|---|
| Insomnia | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Personality change | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood cholesterol increased | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint injury | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Limb injury | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Procedural anxiety | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 4 / 28 (14.29%) | 4 / 30 (13.33%) | 4 / 13 (30.77%) |
| occurrences (all) | 5 | 4 | 4 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 30 (3.33%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 1 | 1 |
| Tension headache | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|---|---|---|
| Hyperaesthesia | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 2 / 30 (6.67%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Eye disorders | | | |
| Dry eye | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Eye pruritus | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 4 / 28 (14.29%) | 4 / 30 (13.33%) | 1 / 13 (7.69%) |
| occurrences (all) | 5 | 4 | 1 |
| Nausea | | | |
| subjects affected / exposed | 3 / 28 (10.71%) | 2 / 30 (6.67%) | 3 / 13 (23.08%) |
| occurrences (all) | 3 | 2 | 3 |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 2 / 30 (6.67%) | 1 / 13 (7.69%) |
| occurrences (all) | 1 | 2 | 1 |
| Constipation | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 1 / 30 (3.33%) | 2 / 13 (15.38%) |
| occurrences (all) | 3 | 1 | 2 |
| Vomiting | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 1 / 30 (3.33%) | 0 / 13 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 1 / 30 (3.33%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Dry mouth | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastrooesophageal reflux disease | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 30 (3.33%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 3 / 28 (10.71%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 2 / 30 (6.67%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Barrett`s oesophagus | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gingival bleeding | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus | | | |
| subjects affected / exposed | 13 / 28 (46.43%) | 6 / 30 (20.00%) | 3 / 13 (23.08%) |
| occurrences (all) | 14 | 6 | 3 |
| Pruritus generalised | | | |
| subjects affected / exposed | 4 / 28 (14.29%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rash papular | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|---|---|---|---|
| Myalgia | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 30 (3.33%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 30 (3.33%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Back pain | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bone pain | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 4 / 28 (14.29%) | 5 / 30 (16.67%) | 1 / 13 (7.69%) |
| occurrences (all) | 5 | 6 | 1 |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 2 / 30 (6.67%) | 0 / 13 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Influenza | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 30 (3.33%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Upper respiratory tract infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 30 (3.33%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abscess neck | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Carbuncle | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infected skin ulcer | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 30 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| **Non-serious adverse events** | OLE Phase: From Cilofexor 100 mg | OLE Phase: From Cilofexor 30 mg | OLE Phase: From Placebo |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 20 / 23 (86.96%) | 25 / 28 (89.29%) | 12 / 12 (100.00%) |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 23 (8.70%) | 0 / 28 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 2 | 0 | 1 |
| Flushing | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 28 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| General disorders and administration site conditions | | | |

| | | | |
|---|---|---|---|
| Fatigue | | | |
| subjects affected / exposed | 3 / 23 (13.04%) | 4 / 28 (14.29%) | 2 / 12 (16.67%) |
| occurrences (all) | 3 | 4 | 2 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 1 / 28 (3.57%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 2 / 23 (8.70%) | 0 / 28 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 2 / 28 (7.14%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Cyst | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 28 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Suprapubic pain | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 28 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Immune system disorders | | | |
| Seasonal allergy | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 28 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 2 / 23 (8.70%) | 2 / 28 (7.14%) | 0 / 12 (0.00%) |
| occurrences (all) | 2 | 3 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 2 / 23 (8.70%) | 0 / 28 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 2 / 28 (7.14%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Personality change | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 28 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|---|---|---|
| Investigations | | | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 1 / 28 (3.57%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 1 | 1 |
| Blood cholesterol increased | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 28 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 0 / 28 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 1 | 0 | 1 |
| Joint injury | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 28 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Limb injury | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 28 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Procedural anxiety | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 28 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 2 / 23 (8.70%) | 1 / 28 (3.57%) | 0 / 12 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 28 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tension headache | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 28 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 2 |
| Hyperaesthesia | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 28 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 23 (8.70%) | 0 / 28 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Eye disorders | | | |
| Dry eye | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 2 / 28 (7.14%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 2 | 1 |
| Eye pruritus | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 28 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 6 / 28 (21.43%) | 4 / 12 (33.33%) |
| occurrences (all) | 1 | 7 | 4 |
| Nausea | | | |
| subjects affected / exposed | 3 / 23 (13.04%) | 2 / 28 (7.14%) | 2 / 12 (16.67%) |
| occurrences (all) | 3 | 2 | 2 |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 3 / 28 (10.71%) | 1 / 12 (8.33%) |
| occurrences (all) | 1 | 4 | 1 |
| Constipation | | | |
| subjects affected / exposed | 2 / 23 (8.70%) | 0 / 28 (0.00%) | 2 / 12 (16.67%) |
| occurrences (all) | 2 | 0 | 2 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 1 / 28 (3.57%) | 1 / 12 (8.33%) |
| occurrences (all) | 1 | 1 | 1 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 0 / 28 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 1 | 0 | 2 |
| Dry mouth | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 2 / 28 (7.14%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 0 / 28 (0.00%) | 2 / 12 (16.67%) |
| occurrences (all) | 1 | 0 | 2 |
| Abdominal distension | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 23 (0.00%) | 2 / 28 (7.14%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 28 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 28 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Barrett`s oesophagus | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 28 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Gingival bleeding | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 28 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus | | | |
| subjects affected / exposed | 4 / 23 (17.39%) | 11 / 28 (39.29%) | 6 / 12 (50.00%) |
| occurrences (all) | 5 | 18 | 7 |
| Pruritus generalised | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 1 / 28 (3.57%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Rash | | | |
| subjects affected / exposed | 2 / 23 (8.70%) | 2 / 28 (7.14%) | 0 / 12 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 0 / 28 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 1 | 0 | 1 |
| Rash papular | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 28 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Myalgia | | | |
| subjects affected / exposed | 3 / 23 (13.04%) | 2 / 28 (7.14%) | 1 / 12 (8.33%) |
| occurrences (all) | 3 | 2 | 1 |
| Pain in extremity | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 23 (8.70%) | 3 / 28 (10.71%) | 1 / 12 (8.33%) |
| occurrences (all) | 2 | 3 | 1 |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 3 / 28 (10.71%) | 2 / 12 (16.67%) |
| occurrences (all) | 1 | 3 | 2 |
| Back pain | | | |
| subjects affected / exposed | 3 / 23 (13.04%) | 0 / 28 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Bone pain | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 28 (0.00%) | 2 / 12 (16.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 28 (0.00%) | 2 / 12 (16.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 1 / 28 (3.57%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 3 / 23 (13.04%) | 4 / 28 (14.29%) | 1 / 12 (8.33%) |
| occurrences (all) | 4 | 6 | 1 |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 23 (8.70%) | 2 / 28 (7.14%) | 2 / 12 (16.67%) |
| occurrences (all) | 2 | 2 | 2 |
| Influenza | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 0 / 28 (0.00%) | 2 / 12 (16.67%) |
| occurrences (all) | 1 | 0 | 2 |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 1 / 28 (3.57%) | 1 / 12 (8.33%) |
| occurrences (all) | 1 | 1 | 1 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 1 / 28 (3.57%) | 1 / 12 (8.33%) |
| occurrences (all) | 1 | 1 | 1 |
| Bronchitis | | | |
| subjects affected / exposed | 2 / 23 (8.70%) | 0 / 28 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 2 | 0 | 1 |

| | | | |
|---|---|---|---|
| Abscess neck | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 28 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Carbuncle | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 28 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 28 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Infected skin ulcer | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 28 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 28 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 28 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 2 |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 30 September 2016 | • Duration of stable ursodeoxycholic acid (UDCA) use was increased from 6 months to 12 months prior to screening to ensure stability of UDCA-induced alkaline phosphatase (ALP) reductions.<br>• Clarification was added that adults with nonalcoholic steatohepatitis should be excluded.<br>• Additional visits were added for safety monitoring during the OLE phase.<br>• New safety and pharmacokinetic (PK) data from nonclinical studies were added.<br>• The risk/benefit assessment was updated with data from a phase 1 study (GS-US-402-1851) reinforcing the positive benefit/risk ratio.<br>• Magnetic resonance elastography was added as an exploratory measure of liver stiffness.<br>• Inclusion criteria for platelet count, albumin, and creatinine clearance (CLcr) were revised to further ensure adults with advanced liver disease would not be enrolled.<br>• Changes to restrictions on concomitant medications were made based on additional drug-drug interaction study data.<br>• Guidelines for drug-induced liver injury (DILI) monitoring and study drug stopping rules were clarified, and creatine phosphokinase (CPK) testing was added.<br>• Preclinical embryofetal toxicity data were added. Requirements for pregnancy testing and contraceptive use were updated. |
| 21 December 2016 | • Final toxicology data were added to support dosing of subjects beyond 12 weeks.<br>• Inclusion criteria were revised to remove CLcr, since serum creatinine was a more appropriate criterion to use in this population.<br>• Concomitant medication guidelines were clarified regarding timing of use of bile acid sequestrants.<br>• Requirements for cirrhosis assessment at screening were clarified.<br>• Frequency of pregnancy testing during the OLE phase was increased. |
| 09 February 2017 | • Elevated ALP as a criterion for close observation for drug-induced liver injury (DILI) was removed, since elevated ALP is one of the characteristics of PBC. Criteria for close observation were clarified. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|---|---|---|
| 04 September 2019 | The study was terminated because of the availability of alternate therapies for primary biliary cholangitis (PBC). | - |

Notes:

## Limitations and caveats

None reported