# Clinical trial results:
# A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Investigate the Efficacy and Safety of Sofosbuvir/GS-5816 Fixed Dose Combination for 12 Weeks in Subjects with Chronic HCV

## Summary

| | |
|---|---|
| EudraCT number | 2014-001683-35 |
| Trial protocol | DE GB IT BE FR |
| Global end of trial date | 23 September 2015 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 07 October 2016 |
| First version publication date | 07 October 2016 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | GS-US-342-1138 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02201940 |
| 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 | Clinical Trial Mailbox, Gilead Sciences International Ltd, ClinicalTrialDisclosures@gilead.com |
| Scientific contact | Clinical Trial Mailbox, Gilead Sciences International Ltd, ClinicalTrialDisclosures@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 | 23 September 2015 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 23 September 2015 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The primary objectives of this study were to evaluate the efficacy, safety, and tolerability of sofosbuvir/velpatasvir (SOF/VEL) fixed-dose combination (FDC) for 12 weeks in adults with chronic genotype 1, 2, 4, 5, or 6 hepatitis C virus (HCV) infection.

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 | 18 July 2014 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Efficacy, Safety |
| Long term follow-up duration | 3 Years |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | United Kingdom: 104 |
| Country: Number of subjects enrolled | Belgium: 45 |
| Country: Number of subjects enrolled | France: 158 |
| Country: Number of subjects enrolled | Germany: 52 |
| Country: Number of subjects enrolled | Italy: 18 |
| Country: Number of subjects enrolled | Canada: 62 |
| Country: Number of subjects enrolled | United States: 279 |
| Country: Number of subjects enrolled | China: 23 |
| Worldwide total number of subjects | 741 |
| EEA total number of subjects | 377 |

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) | 641 |
| From 65 to 84 years | 100 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Participants were enrolled at study sites in the United States, Canada, Europe, and Asia. The first participant was screened on 18 July 2014. The last study visit occurred on 23 September 2015.

### Pre-assignment

Screening details:

847 participants were screened.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | SOF/VEL |

Arm description:

SOF/VEL for 12 weeks

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Sofosbuvir/velpatasvir |
| Investigational medicinal product code | |
| Other name | Epclusa®, GS-7977/GS-5816 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

400/100 mg FDC tablet administered once daily

| | |
|---|---|
| **Arm title** | Placebo |

Arm description:

SOF/VEL placebo for 12 weeks

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

Dosage and administration details:

Placebo tablet administered once daily

| **Number of subjects in period 1[1]** | SOF/VEL | Placebo |
|---|---|---|
| Started | 624 | 116 |
| Completed | 613 | 0 |
| Not completed | 11 | 116 |
| Withdrew Consent | 2 | 1 |
| Adverse event, non-fatal | - | 1 |
| Death | 1 | - |
| Investigator's Discretion | 1 | 1 |
| Lost to follow-up | 5 | - |
| Lack of efficacy | 2 | 113 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 1 participant who was enrolled but not treated is not included in the subject disposition table.

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | SOF/VEL |
| Reporting group description: SOF/VEL for 12 weeks | |
| Reporting group title | Placebo |
| Reporting group description: SOF/VEL placebo for 12 weeks | |

| Reporting group values | SOF/VEL | Placebo | Total |
|---|---|---|---|
| Number of subjects | 624 | 116 | 740 |
| Age categorical<br>Units: Subjects | | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 54 | 53 | |
| standard deviation | ± 10.9 | ± 10.4 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 250 | 48 | 298 |
| Male | 374 | 68 | 442 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 31 | 5 | 36 |
| Not Hispanic or Latino | 589 | 111 | 700 |
| Not Disclosed | 4 | 0 | 4 |
| Race<br>Units: Subjects | | | |
| Black or African American | 52 | 12 | 64 |
| White | 493 | 89 | 582 |
| Asian | 62 | 11 | 73 |
| American Indian/ Alaska Native | 7 | 0 | 7 |
| Hawaiian or Pacific Islander | 1 | 1 | 2 |
| Other | 6 | 3 | 9 |
| Not Disclosed | 3 | 0 | 3 |
| HCV Genotype<br>Units: Subjects | | | |
| Genotype 1 | 328 | 65 | 393 |
| Genotype 2 | 104 | 21 | 125 |
| Genotype 4 | 116 | 22 | 138 |
| Genotype 5 | 35 | 0 | 35 |
| Genotype 6 | 41 | 8 | 49 |
| IL28b Status | | | |
| CC, CT, and TT alleles are different forms of the IL28b gene. | | | |
| Units: Subjects | | | |
| CC | 186 | 36 | 222 |

| | | | |
|---|---|---|---|
| CT | 339 | 53 | 392 |
| TT | 94 | 26 | 120 |
| Missing | 5 | 1 | 6 |
| HCV RNA Category<br>Units: Subjects | | | |
| < 800,000 IU/mL | 163 | 29 | 192 |
| ≥ 800,000 IU/mL | 461 | 87 | 548 |
| Cirrhosis Status<br>Units: Subjects | | | |
| Present | 121 | 21 | 142 |
| Absent | 501 | 95 | 596 |
| Missing | 2 | 0 | 2 |
| HCV RNA<br>Units: log10 IU/mL | | | |
| arithmetic mean | 6.3 | 6.3 | |
| standard deviation | ± 0.66 | ± 0.58 | - |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | SOF/VEL |
| Reporting group description: SOF/VEL for 12 weeks | |
| Reporting group title | Placebo |
| Reporting group description: SOF/VEL placebo for 12 weeks | |

### Primary: Percentage of Participants With Sustained Virologic Response (SVR) 12 Weeks After Discontinuation of Therapy (SVR12)

| | |
|---|---|
| End point title | Percentage of Participants With Sustained Virologic Response (SVR) 12 Weeks After Discontinuation of Therapy (SVR12)[1] |

End point description:

SVR12 was defined as HCV RNA < the lower limit of quantitation (LLOQ; ie, 15 IU/mL) at 12 weeks after stopping study treatment.

Full Analysis Set: participants randomized or enrolled into the study and received at least 1 dose of study drug.

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

End point timeframe:

Posttreatment Week 12

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: Statistical analysis was performed against a performance goal of 85% and not between the treatment groups.

| End point values | SOF/VEL | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 624 | 116 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 99 (97.9 to 99.6) | 0 (0 to 3.1) | | |

### Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of Participants Who Permanently Discontinued Any Study Drug Due to an Adverse Event

| | |
|---|---|
| End point title | Percentage of Participants Who Permanently Discontinued Any Study Drug Due to an Adverse Event[2] |

End point description:

Safety Analysis Set: participants who received at least 1 dose of study drug.

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

End point timeframe:

Up to 12 weeks

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** | SOF/VEL | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 624 | 116 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 0.2 | 1.7 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With SVR at 4 and 24 Weeks After Discontinuation of Therapy (SVR4 and SVR24)

| End point title | Percentage of Participants With SVR at 4 and 24 Weeks After Discontinuation of Therapy (SVR4 and SVR24) |
|---|---|

End point description:

SVR4 and SVR 24 were defined as HCV RNA < LLOQ at 4 and 24 weeks after stopping study treatment, respectively.

Full Analysis Set

| End point type | Secondary |
|---|---|

End point timeframe:

Posttreatment Weeks 4 and 24

| **End point values** | SOF/VEL | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 624 | 116 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| SVR4 | 99.2 (98.1 to 99.7) | 0 (0 to 3.1) | | |
| SVR24 | 99 (97.9 to 99.6) | 0 (0 to 3.1) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With HCV RNA < LLOQ at Weeks 1, 2, 4, 6, 8, 10, and 12

| End point title | Percentage of Participants With HCV RNA < LLOQ at Weeks 1, 2, 4, 6, 8, 10, and 12 |
|---|---|

| | |
|---|---|
| End point description: | |
| Participants in the Full Analysis Set with available data were analyzed. | |
| End point type | Secondary |
| End point timeframe: | |
| Weeks 1, 2, 4, 6, 8, 10, and 12 | |

| **End point values** | SOF/VEL | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 624 | 116 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Week 1 (SOF/VEL: N = 624; Placebo: N = 116) | 18.8 (15.8 to 22) | 0 (0 to 3.1) | | |
| Week 2 (SOF/VEL: N = 624; Placebo: N = 116) | 56.9 (52.9 to 60.8) | 0 (0 to 3.1) | | |
| Week 4 (SOF/VEL: N = 623; Placebo: N = 116) | 90.5 (88 to 92.7) | 0 (0 to 3.1) | | |
| Week 6 (SOF/VEL: N = 623; Placebo: N = 115) | 98.9 (97.7 to 99.5) | 0 (0 to 3.2) | | |
| Week 8 (SOF/VEL: N = 622; Placebo: N = 114) | 99.7 (98.8 to 100) | 0 (0 to 3.2) | | |
| Week 10 (SOF/VEL: N = 622; Placebo: N = 114) | 100 (99.4 to 100) | 0 (0 to 3.2) | | |
| Week 12 (SOF/VEL: N = 622; Placebo: N = 113) | 100 (99.4 to 100) | 0 (0 to 3.2) | | |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Change From Baseline in HCV RNA at Weeks 1, 2, 4, 6, 8, 10, and 12**

| | |
|---|---|
| End point title | Change From Baseline in HCV RNA at Weeks 1, 2, 4, 6, 8, 10, and 12 |
| End point description: | |
| Participants in the Full Analysis Set with available data were analyzed. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline; Weeks 1, 2, 4, 6, 8, 10, and 12 | |

| **End point values** | SOF/VEL | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 624 | 116 | | |
| Units: log10 IU/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Wk 1 (SOF/VEL: N= 617; Placebo: N= 114) | -4.29 (± 0.647) | -0.05 (± 0.561) | | |

| | | | | |
|---|---|---|---|---|
| Change at Wk 2 (SOF/VEL: N= 622; Placebo: N= 116) | -4.82 (± 0.685) | 0.01 (± 0.28) | | |
| Change at Wk 4 (SOF/VEL: N= 617; Placebo: N= 114) | -5.08 (± 0.656) | -0.01 (± 0.297) | | |
| Change at Wk 6 (SOF/VEL: N= 623; Placebo: N= 115) | -5.11 (± 0.664) | 0.07 (± 0.298) | | |
| Change at Wk 8 (SOF/VEL: N= 622; Placebo: N= 113) | -5.11 (± 0.664) | 0.05 (± 0.281) | | |
| Change at Wk 10 (SOF/VEL: N= 622; Placebo: N= 112) | -5.12 (± 0.662) | 0.05 (± 0.337) | | |
| Change at Wk 12 (SOF/VEL: N= 622; Placebo: N= 111) | -5.12 (± 0.662) | -0.06 (± 0.58) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With Virologic Failure

| End point title | Percentage of Participants With Virologic Failure |
|---|---|

End point description:

Virologic failure was defined as:
1) On-treatment virologic failure:
• Breakthrough (confirmed HCV RNA ≥ LLOQ after having previously had HCV RNA < LLOQ while on treatment), or
• Rebound (confirmed > 1 log10 IU/mL increase in HCV RNA from nadir while on treatment), or
• Non-response (HCV RNA persistently ≥ LLOQ through 8 weeks of treatment), OR
2) Virologic relapse:
• Confirmed HCV RNA ≥ LLOQ during the posttreatment period having achieved HCV RNA < LLOQ at last ontreatment visit.

Full Analysis Set

| End point type | Secondary |
|---|---|

End point timeframe:

Up to Posttreatment Week 24

| End point values | SOF/VEL | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 624 | 116 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 0.3 | 100 | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: Up to 12 weeks plus 30 days | |
| Assessment type | Systematic |
| **Dictionary used** | |
| Dictionary name | MedDRA |
| Dictionary version | 18.0 |
| **Reporting groups** | |
| Reporting group title | SOF/VEL |
| Reporting group description: SOF/VEL for 12 weeks | |
| Reporting group title | Placebo |
| Reporting group description: SOF/VEL placebo for 12 weeks | |

| Serious adverse events | SOF/VEL | Placebo | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 15 / 624 (2.40%) | 0 / 116 (0.00%) | |
| number of deaths (all causes) | 1 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Lung neoplasm malignant | | | |
| subjects affected / exposed | 1 / 624 (0.16%) | 0 / 116 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Ligament sprain | | | |
| subjects affected / exposed | 1 / 624 (0.16%) | 0 / 116 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper limb fracture | | | |
| subjects affected / exposed | 1 / 624 (0.16%) | 0 / 116 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |

| | | | |
|---|---|---|---|
| Extremity necrosis | | | |
| subjects affected / exposed | 1 / 624 (0.16%) | 0 / 116 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 624 (0.16%) | 0 / 116 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Palpitations | | | |
| subjects affected / exposed | 1 / 624 (0.16%) | 0 / 116 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Epilepsy | | | |
| subjects affected / exposed | 1 / 624 (0.16%) | 0 / 116 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Sudden death | | | |
| subjects affected / exposed | 1 / 624 (0.16%) | 0 / 116 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 1 / 624 (0.16%) | 0 / 116 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 1 / 624 (0.16%) | 0 / 116 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |

| | | | |
|---|---|---|---|
| Mania | | | |
| subjects affected / exposed | 1 / 624 (0.16%) | 0 / 116 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Rotator cuff syndrome | | | |
| subjects affected / exposed | 1 / 624 (0.16%) | 0 / 116 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Abscess limb | | | |
| subjects affected / exposed | 1 / 624 (0.16%) | 0 / 116 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 624 (0.16%) | 0 / 116 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 624 (0.16%) | 0 / 116 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 624 (0.16%) | 0 / 116 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 624 (0.16%) | 0 / 116 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza | | | |
| subjects affected / exposed | 1 / 624 (0.16%) | 0 / 116 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Vestibular neuronitis | | | |
| subjects affected / exposed | 1 / 624 (0.16%) | 0 / 116 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | SOF/VEL | Placebo | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 393 / 624 (62.98%) | 77 / 116 (66.38%) | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 182 / 624 (29.17%) | 33 / 116 (28.45%) | |
| occurrences (all) | 236 | 39 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 127 / 624 (20.35%) | 24 / 116 (20.69%) | |
| occurrences (all) | 132 | 26 | |
| Asthenia | | | |
| subjects affected / exposed | 42 / 624 (6.73%) | 9 / 116 (7.76%) | |
| occurrences (all) | 46 | 9 | |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 75 / 624 (12.02%) | 13 / 116 (11.21%) | |
| occurrences (all) | 80 | 14 | |
| Diarrhoea | | | |
| subjects affected / exposed | 48 / 624 (7.69%) | 8 / 116 (6.90%) | |
| occurrences (all) | 53 | 8 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 39 / 624 (6.25%) | 4 / 116 (3.45%) | |
| occurrences (all) | 41 | 5 | |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 50 / 624 (8.01%) | 11 / 116 (9.48%) | |
| occurrences (all) | 51 | 12 | |

| | | | |
|---|---|---|---|
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 40 / 624 (6.41%) | 9 / 116 (7.76%) | |
| occurrences (all) | 41 | 11 | |
| Back pain | | | |
| subjects affected / exposed | 29 / 624 (4.65%) | 11 / 116 (9.48%) | |
| occurrences (all) | 29 | 12 | |
| Myalgia | | | |
| subjects affected / exposed | 25 / 624 (4.01%) | 6 / 116 (5.17%) | |
| occurrences (all) | 27 | 6 | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 80 / 624 (12.82%) | 12 / 116 (10.34%) | |
| occurrences (all) | 87 | 14 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

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

| |
|---|
| There were no limitations affecting the analysis or results. |

Notes: