

**Clinical trial results:****A Phase 3, Global, Multicenter, Randomized, Open-Label Study to Investigate the Safety and Efficacy of Sofosbuvir/Velpatasvir/GS-9857 Fixed-Dose Combination for 8 Weeks Compared to Sofosbuvir/Velpatasvir for 12 Weeks in Direct-Acting Antiviral-Naive Subjects with Chronic HCV Infection****Summary**

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2015-003460-36  |
| Trial protocol           | DE GB FR        |
| Global end of trial date | 11 January 2017 |

**Results information**

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 16 December 2017 |
| First version publication date | 16 December 2017 |

**Trial information****Trial identification**

|                       |                |
|-----------------------|----------------|
| Sponsor protocol code | GS-US-367-1172 |
|-----------------------|----------------|

**Additional study identifiers**

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02607800 |
| 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 Trials Mailbox, Gilead Sciences International Ltd.,<br>ClinicalTrialDisclosures@gilead.com |
| Scientific contact           | Clinical Trials Mailbox, Gilead Sciences International Ltd.,<br>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                       | 11 January 2017 |
| Is this the analysis of the primary completion data? | No              |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 11 January 2017 |
| 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 compare the efficacy, safety, and tolerability of treatment with sofosbuvir/velpatasvir/voxilaprevir (SOF/VEL/VOX) fixed dose combination (FDC) for 8 weeks with that of SOF/VEL FDC for 12 weeks in direct-acting antiviral-naive participants with chronic 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                          | 16 November 2015 |
| 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 Kingdom: 47 |
| Country: Number of subjects enrolled | France: 187        |
| Country: Number of subjects enrolled | Germany: 45        |
| Country: Number of subjects enrolled | New Zealand: 26    |
| Country: Number of subjects enrolled | Canada: 60         |
| Country: Number of subjects enrolled | Australia: 24      |
| Country: Number of subjects enrolled | United States: 554 |
| Worldwide total number of subjects   | 943                |
| EEA total number of subjects         | 279                |

Notes:

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**Subjects enrolled per age group**

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|   |     |
|---|-----|
| 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)                      | 849 |
| From 65 to 84 years                       | 94  |
| 85 years and over                         | 0   |

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## Subject disposition

### Recruitment

Recruitment details:

Participants were enrolled at study sites in North America, Europe, and Asia Pacific. The first participant was screened on 16 November 2015. The last study visit occurred on 11 January 2017.

### Pre-assignment

Screening details:

1116 participants were screened.

### Period 1

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

### Arms

|                              |                     |
|------------------------------|---------------------|
| Are arms mutually exclusive? | Yes                 |
| <b>Arm title</b>             | SOF/VEL/VOX 8 Weeks |

Arm description:

SOF/VEL/VOX (400/100/100 mg) FDC tablet orally once daily with food for 8 weeks

|  |                                     |
|--|-------------------------------------|
| Arm type                               | Experimental                        |
| Investigational medicinal product name | Sofosbuvir/Velpatasvir/Voxilaprevir |
| Investigational medicinal product code |                                     |
| Other name                             | Vosevi®, SOF/VEL/VOX                |
| Pharmaceutical forms                   | Tablet                              |
| Routes of administration               | Oral use                            |

Dosage and administration details:

400/100/100 mg once daily with food for 8 weeks

|                  |                  |
|------------------|------------------|
| <b>Arm title</b> | SOF/VEL 12 Weeks |
|------------------|------------------|

Arm description:

SOF/VEL (400/100 mg) FDC tablet orally once daily with or without food for 12 weeks

|  |                        |
|--|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | Sofosbuvir/Velpatasvir |
| Investigational medicinal product code |                        |
| Other name                             | Epclusa®; SOF/VEL      |
| Pharmaceutical forms                   | Tablet                 |
| Routes of administration               | Oral use               |

Dosage and administration details:

400/100 mg FDC once daily with or without food for 12 weeks

| <b>Number of subjects in period 1</b> <sup>[1]</sup> | SOF/VEL/VOX 8 Weeks | SOF/VEL 12 Weeks |
|--|---------------------|------------------|
| Started  | 501                 | 440              |
| Completed  | 492                 | 430              |
| Not completed  | 9                   | 10               |
| Withdrew Consent                                     | 2                   | -                |

|                   |   |    |
|-------------------|---|----|
| Lost to follow-up | 7 | 10 |
|-------------------|---|----|

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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: 2 participants (one in each treatment group) who were randomized but not treated are not included in the subject disposition table.

## Baseline characteristics

### Reporting groups

|   |                     |
|---|---------------------|
| Reporting group title   | SOF/VEL/VOX 8 Weeks |
| Reporting group description:<br>SOF/VEL/VOX (400/100/100 mg) FDC tablet orally once daily with food for 8 weeks     |                     |
| Reporting group title   | SOF/VEL 12 Weeks    |
| Reporting group description:<br>SOF/VEL (400/100 mg) FDC tablet orally once daily with or without food for 12 weeks |                     |

| Reporting group values  | SOF/VEL/VOX 8 Weeks | SOF/VEL 12 Weeks | Total |
|---|---------------------|------------------|-------|
| Number of subjects  | 501                 | 440              | 941   |
| Age categorical<br>Units: Subjects                                |                     |                  |       |
| Age continuous<br>Units: years                                    |                     |                  |       |
| arithmetic mean   | 53                  | 52               | -     |
| standard deviation  | ± 11.1              | ± 11.9           |       |
| Gender categorical<br>Units: Subjects                             |                     |                  |       |
| Female  | 246                 | 203              | 449   |
| Male  | 255                 | 237              | 492   |
| Race<br>Units: Subjects   |                     |                  |       |
| White   | 391                 | 365              | 756   |
| Black or African American   | 48                  | 47               | 95    |
| Asian   | 51                  | 22               | 73    |
| Other   | 5                   | 2                | 7     |
| American Indian or Alaska Native                                  | 3                   | 2                | 5     |
| Native Hawaiian or Pacific Islander                               | 3                   | 2                | 5     |
| Ethnicity<br>Units: Subjects                                      |                     |                  |       |
| Hispanic or Latino  | 32                  | 52               | 84    |
| Not Hispanic or Latino  | 469                 | 388              | 857   |
| IL28b Status  |                     |                  |       |
| The CC, CT, and TT alleles are different forms of the IL28b gene. |                     |                  |       |
| Units: Subjects   |                     |                  |       |
| CC  | 166                 | 136              | 302   |
| CT  | 253                 | 245              | 498   |
| TT  | 82                  | 59               | 141   |
| HCV RNA Category<br>Units: Subjects                               |                     |                  |       |
| < 800,000 IU/mL   | 155                 | 138              | 293   |
| ≥ 800,000 IU/mL   | 346                 | 302              | 648   |

|                                |        |        |   |
|--------------------------------|--------|--------|---|
| HCV RNA                        |        |        |   |
| Units: log <sub>10</sub> IU/mL |        |        |   |
| arithmetic mean                | 6.1    | 6.2    |   |
| standard deviation             | ± 0.75 | ± 0.66 | - |

## End points

### End points reporting groups

|                              |   |
|------------------------------|---|
| Reporting group title        | SOF/VEL/VOX 8 Weeks   |
| Reporting group description: | SOF/VEL/VOX (400/100/100 mg) FDC tablet orally once daily with food for 8 weeks     |
| Reporting group title        | SOF/VEL 12 Weeks  |
| Reporting group description: | SOF/VEL (400/100 mg) FDC tablet orally once daily with or without food 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)  |
| End point description: | 1) SVR12 was defined as HCV RNA < the lower limit of quantitation (LLOQ) at 12 weeks after stopping study treatment.<br>2) Full Analysis Set: all randomized/enrolled participants who took at least 1 dose of the study drug |
| End point type         | Primary   |
| End point timeframe:   | Posttreatment Week 12   |

| End point values                  | SOF/VEL/VOX 8 Weeks | SOF/VEL 12 Weeks    |  |  |
|-----------------------------------|---------------------|---------------------|--|--|
| Subject group type                | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed       | 501                 | 440                 |  |  |
| Units: percentage of participants |                     |                     |  |  |
| number (confidence interval 95%)  | 95.2 (93.0 to 96.9) | 98.2 (96.4 to 99.2) |  |  |

### Statistical analyses

|   |   |
|---|---|
| Statistical analysis title              | SVR12 – SOF/VEL/VOX 8 Weeks vs SOF/VEL 12 Weeks |
| Comparison groups                       | SOF/VEL 12 Weeks v SOF/VEL/VOX 8 Weeks          |
| Number of subjects included in analysis | 941   |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | non-inferiority <sup>[1]</sup>                  |
| Parameter estimate                      | Difference in proportions                       |
| Point estimate                          | -3.2  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -6  |
| upper limit                             | -0.4  |

Notes:

[1] - Noninferiority was demonstrated if the lower bound of the 2-sided 95% confidence interval (CI) for the difference in SVR12 was greater than -5%. If the lower bound of the CI was greater than -5% (ie, the noninferiority null hypothesis was rejected), a 2-sided stratified Cochran-Mantel-Haenszel test was to be used to test for the superiority of SOF/VEL/VOX for 8 weeks over SOF/VEL for 12 weeks at a significance level of 0.05.

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

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Who Permanently Discontinue Study Drug Due to an Adverse Event <sup>[2]</sup> |
|-----------------|--|

End point description:

Safety Analysis Set

|                |         |
|----------------|---------|
| 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/VOX<br>8 Weeks | SOF/VEL 12<br>Weeks |  |  |
|-----------------------------------|------------------------|---------------------|--|--|
| Subject group type                | Reporting group        | Reporting group     |  |  |
| Number of subjects analysed       | 501                    | 440                 |  |  |
| Units: percentage of participants |                        |                     |  |  |
| number (not applicable)           | 0                      | 0.5                 |  |  |

### 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:

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

2) Full Analysis Set

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

End point timeframe:

Posttreatment Weeks 4 and 24

| <b>End point values</b>           | SOF/VEL/VOX<br>8 Weeks | SOF/VEL 12<br>Weeks    |  |  |
|-----------------------------------|------------------------|------------------------|--|--|
| Subject group type                | Reporting group        | Reporting group        |  |  |
| Number of subjects analysed       | 501                    | 440                    |  |  |
| Units: percentage of participants |                        |                        |  |  |
| number (confidence interval 95%)  |                        |                        |  |  |
| SVR4                              | 96.4 (94.4 to<br>97.9) | 98.9 (97.4 to<br>99.6) |  |  |
| SVR24                             | 95.0 (92.7 to<br>96.7) | 98.0 (96.2 to<br>99.1) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants With HCV RNA < LLOQ On Treatment

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants With HCV RNA < LLOQ On Treatment |
|-----------------|---|

End point description:

- 1) Percentage of participants in Full Analysis Set with on-treatment data were analyzed.
- 2) 999 = Not Applicable (NA) (The treatment for this group was only 8 weeks.)

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

End point timeframe:

Posttreatment Weeks 4 and 24

| <b>End point values</b>                           | SOF/VEL/VOX<br>8 Weeks | SOF/VEL 12<br>Weeks     |  |  |
|---|------------------------|-------------------------|--|--|
| Subject group type                                | Reporting group        | Reporting group         |  |  |
| Number of subjects analysed                       | 501                    | 440                     |  |  |
| Units: percentage of participants                 |                        |                         |  |  |
| number (confidence interval 95%)                  |                        |                         |  |  |
| Week 1 (SOF/VEL/VOX: N = 501;<br>SOF/VEL: N= 440) | 24.8 (21.0 to<br>28.8) | 22.7 (18.9 to<br>26.9)  |  |  |
| Week 2 (SOF/VEL/VOX: N = 501;<br>SOF/VEL: N= 439) | 65.9 (61.5 to<br>70.0) | 61.3 (56.5 to<br>65.9)  |  |  |
| Week 4 (SOF/VEL/VOX: N = 501;<br>SOF/VEL:N= 439)  | 92.4 (89.7 to<br>94.6) | 92.0 (89.1 to<br>94.4)  |  |  |
| Week 8 (SOF/VEL/VOX: N = 500;<br>SOF/VEL: N= 439) | 99.2 (98.0 to<br>99.8) | 99.8 (98.7 to<br>100.0) |  |  |
| Week 12 (SOF/VEL/VOX: N =NA;<br>SOF/VEL: N= 439)  | 999 (999 to<br>999)    | 99.8 (98.7 to<br>100.0) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in HCV RNA

|  |                                 |
|--|---------------------------------|
| End point title  | Change From Baseline in HCV RNA |
| End point description:   |                                 |
| 1) Participants in the Full Analysis Set with available data were analyzed.<br>2) 999 = Not Applicable (NA) (The treatment for this group was only 8 weeks.) |                                 |
| End point type   | Secondary                       |
| End point timeframe:   |                                 |
| Up to 12 weeks   |                                 |

| End point values                                  | SOF/VEL/VOX<br>8 Weeks | SOF/VEL 12<br>Weeks |  |  |
|---|------------------------|---------------------|--|--|
| Subject group type                                | Reporting group        | Reporting group     |  |  |
| Number of subjects analysed                       | 501                    | 440                 |  |  |
| Units: log10 IU/mL                                |                        |                     |  |  |
| arithmetic mean (standard deviation)              |                        |                     |  |  |
| Week 1 (SOF/VEL/VOX: N = 491;<br>SOF/VEL: N= 433) | -4.23 (±<br>0.689)     | -4.24 (±<br>0.679)  |  |  |
| Week 2 (SOF/VEL/VOX: N = 496;<br>SOF/VEL: N= 436) | -4.75 (±<br>0.747)     | -4.77 (±<br>0.646)  |  |  |
| Week 4 (SOF/VEL/VOX: N = 501;<br>SOF/VEL: N= 437) | -4.95 (± 0.75)         | -4.99 (±<br>0.656)  |  |  |
| Week 8 (SOF/VEL/VOX: N = 496;<br>SOF/VEL: N= 439) | -4.99 (±<br>0.754)     | -5.03 (±<br>0.655)  |  |  |
| Week 12 (SOF/VEL/VOX: N = NA;<br>SOF/VEL: N= 438) | 999 (± 999)            | -5.03 (±<br>0.656)  |  |  |

## 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 is defined as:   |   |
| 1) On-treatment virologic failure:   |   |
| a) Breakthrough (confirmed HCV RNA $\geq$ LLOQ after having previously had HCV RNA $<$ LLOQ while on treatment), or          |   |
| b) Rebound (confirmed $>$ 1 log10 IU/mL increase in HCV RNA from nadir while on treatment), or                               |   |
| c) Non-response (HCV RNA persistently $\geq$ LLOQ through 8 weeks of treatment)  |   |
| 2) Virologic relapse:  |   |
| a) Confirmed HCV RNA $\geq$ LLOQ during the posttreatment period having achieved HCV RNA $<$ LLOQ at last on-treatment visit |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| Up to Posttreatment Week 24  |   |

| <b>End point values</b>           | SOF/VEL/VOX<br>8 Weeks | SOF/VEL 12<br>Weeks |  |  |
|-----------------------------------|------------------------|---------------------|--|--|
| Subject group type                | Reporting group        | Reporting group     |  |  |
| Number of subjects analysed       | 501                    | 440                 |  |  |
| Units: percentage of participants |                        |                     |  |  |
| number (not applicable)           | 4.2                    | 0.7                 |  |  |

### **Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 12 weeks plus 30 days

Adverse event reporting additional description:

Safety Analysis Set

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

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 19.0 |
|--------------------|------|

### Reporting groups

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | SOF/VEL/VOX 8 Weeks |
|-----------------------|---------------------|

Reporting group description:

SOF/VEL/VOX (400/100/100 mg) FDC tablet orally once daily with food for 8 weeks

|                       |                  |
|-----------------------|------------------|
| Reporting group title | SOF/VEL 12 Weeks |
|-----------------------|------------------|

Reporting group description:

SOF/VEL ( 400/100 mg) FDC tablet orally once daily with or without food for 12 weeks

| <b>Serious adverse events</b>                                       | SOF/VEL/VOX 8 Weeks | SOF/VEL 12 Weeks |  |
|---|---------------------|------------------|--|
| Total subjects affected by serious adverse events                   |                     |                  |  |
| subjects affected / exposed   | 15 / 501 (2.99%)    | 7 / 440 (1.59%)  |  |
| number of deaths (all causes)                                       | 0                   | 0                |  |
| number of deaths resulting from adverse events                      | 0                   | 0                |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                     |                  |  |
| Breast cancer   |                     |                  |  |
| subjects affected / exposed   | 1 / 501 (0.20%)     | 0 / 440 (0.00%)  |  |
| occurrences causally related to treatment / all                     | 0 / 1               | 0 / 0            |  |
| deaths causally related to treatment / all                          | 0 / 0               | 0 / 0            |  |
| Lung adenocarcinoma metastatic                                      |                     |                  |  |
| subjects affected / exposed   | 1 / 501 (0.20%)     | 0 / 440 (0.00%)  |  |
| occurrences causally related to treatment / all                     | 0 / 1               | 0 / 0            |  |
| deaths causally related to treatment / all                          | 0 / 0               | 0 / 0            |  |
| Vascular disorders  |                     |                  |  |
| Peripheral artery occlusion   |                     |                  |  |
| subjects affected / exposed   | 1 / 501 (0.20%)     | 0 / 440 (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 |                 |                 |  |
| Chest pain   |                 |                 |  |
| subjects affected / exposed                          | 1 / 501 (0.20%) | 0 / 440 (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      |                 |                 |  |
| Asthma   |                 |                 |  |
| subjects affected / exposed                          | 1 / 501 (0.20%) | 0 / 440 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Psychiatric disorders                                |                 |                 |  |
| Alcohol withdrawal syndrome                          |                 |                 |  |
| subjects affected / exposed                          | 0 / 501 (0.00%) | 1 / 440 (0.23%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Depression   |                 |                 |  |
| subjects affected / exposed                          | 0 / 501 (0.00%) | 1 / 440 (0.23%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Suicide attempt                                      |                 |                 |  |
| subjects affected / exposed                          | 0 / 501 (0.00%) | 1 / 440 (0.23%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Injury, poisoning and procedural complications       |                 |                 |  |
| Multiple fractures                                   |                 |                 |  |
| subjects affected / exposed                          | 0 / 501 (0.00%) | 1 / 440 (0.23%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Road traffic accident                                |                 |                 |  |
| subjects affected / exposed                          | 0 / 501 (0.00%) | 1 / 440 (0.23%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Cardiac disorders                                    |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Acute myocardial infarction                     |                 |                 |  |
| subjects affected / exposed                     | 1 / 501 (0.20%) | 0 / 440 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Angina pectoris                                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 501 (0.00%) | 1 / 440 (0.23%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Atrial fibrillation                             |                 |                 |  |
| subjects affected / exposed                     | 1 / 501 (0.20%) | 0 / 440 (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                        |                 |                 |  |
| Cerebral haemorrhage                            |                 |                 |  |
| subjects affected / exposed                     | 1 / 501 (0.20%) | 0 / 440 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastrointestinal disorders                      |                 |                 |  |
| Small intestinal obstruction                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 501 (0.20%) | 0 / 440 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hepatobiliary disorders                         |                 |                 |  |
| Biliary colic                                   |                 |                 |  |
| subjects affected / exposed                     | 1 / 501 (0.20%) | 0 / 440 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cholelithiasis                                  |                 |                 |  |
| subjects affected / exposed                     | 1 / 501 (0.20%) | 0 / 440 (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 |                 |                 |  |
| Back pain                                       |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 501 (0.20%) | 0 / 440 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Flank pain</b>                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 501 (0.00%) | 1 / 440 (0.23%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Musculoskeletal chest pain</b>               |                 |                 |  |
| subjects affected / exposed                     | 1 / 501 (0.20%) | 0 / 440 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Infections and infestations</b>              |                 |                 |  |
| <b>Clostridium difficile colitis</b>            |                 |                 |  |
| subjects affected / exposed                     | 0 / 501 (0.00%) | 1 / 440 (0.23%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Perineal abscess</b>                         |                 |                 |  |
| subjects affected / exposed                     | 1 / 501 (0.20%) | 0 / 440 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Pneumonia</b>                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 501 (0.00%) | 1 / 440 (0.23%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Pyelonephritis</b>                           |                 |                 |  |
| subjects affected / exposed                     | 1 / 501 (0.20%) | 1 / 440 (0.23%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Metabolism and nutrition disorders</b>       |                 |                 |  |
| <b>Myositis</b>                                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 501 (0.00%) | 1 / 440 (0.23%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

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

| <b>Non-serious adverse events</b>   | SOF/VEL/VOX 8 Weeks                                     | SOF/VEL 12 Weeks                                      |  |
|---|---|---|--|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed  | 280 / 501 (55.89%)                                      | 213 / 440 (48.41%)                                    |  |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)  | 134 / 501 (26.75%)<br>150                               | 99 / 440 (22.50%)<br>112                              |  |
| General disorders and administration site conditions<br>Asthenia<br>subjects affected / exposed<br>occurrences (all)<br><br>Fatigue<br>subjects affected / exposed<br>occurrences (all) | 32 / 501 (6.39%)<br>35<br><br>106 / 501 (21.16%)<br>114 | 27 / 440 (6.14%)<br>27<br><br>91 / 440 (20.68%)<br>93 |  |
| Gastrointestinal disorders<br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Nausea<br>subjects affected / exposed<br>occurrences (all)                           | 88 / 501 (17.56%)<br>98<br><br>80 / 501 (15.97%)<br>83  | 32 / 440 (7.27%)<br>36<br><br>40 / 440 (9.09%)<br>45  |  |
| Psychiatric disorders<br>Insomnia<br>subjects affected / exposed<br>occurrences (all)   | 26 / 501 (5.19%)<br>28                                  | 21 / 440 (4.77%)<br>21                                |  |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all)   | 19 / 501 (3.79%)<br>19                                  | 24 / 440 (5.45%)<br>25                                |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment  |
|-----------------|--|
| 09 October 2015 | <ol style="list-style-type: none"><li>1. Removed all references to genotype 3 cirrhotic subjects and clarified that these subjects will not be enrolled in this study, but rather will be included in GS-US-367-1173</li><li>2. The total number of study centers participating were increased from 100 to 120.</li><li>3. Revisions were made to the approximate number of subjects by genotype to be randomized or enrolled into each group.</li><li>4. Updates were made to Rationale for This Study, Rationale for the Study Design, and Risk/Benefit Assessment for the Study to account for study changes and provide clarification.</li><li>5. Additional formatting, minor grammatical corrections, and updates were made.</li></ol> |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/28390869>