



## Clinical trial results:

### A Phase 3, Global, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Investigate the Safety and Efficacy of Sofosbuvir/Velpatasvir/GS-9857 Fixed-Dose Combination for 12 Weeks in Direct-Acting Antiviral-Experienced Subjects with Chronic HCV Infection

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2015-003455-21 |
| Trial protocol           | DE GB FR       |
| Global end of trial date | 21 June 2017   |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1           |
| This version publication date  | 01 July 2018 |
| First version publication date | 01 July 2018 |

#### Trial information

##### Trial identification

|                       |                |
|-----------------------|----------------|
| Sponsor protocol code | GS-US-367-1171 |
|-----------------------|----------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02607735 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Gilead Sciences  |
| Sponsor organisation address | 333 Lakeside Drive, Foster City, 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                       | 21 June 2017    |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 10 October 2016 |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 21 June 2017    |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

The primary objectives of this study are to evaluate the safety and efficacy of treatment with sofosbuvir/velpatasvir/voxilaprevir (SOF/VEL/VOX) in adults with chronic Hepatitis C Virus (HCV) infection who have previously received treatment with direct-acting antiviral therapy.

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                          | 11 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: 9  |
| Country: Number of subjects enrolled | France: 72         |
| Country: Number of subjects enrolled | Germany: 23        |
| Country: Number of subjects enrolled | United States: 237 |
| Country: Number of subjects enrolled | Canada: 42         |
| Country: Number of subjects enrolled | Australia: 26      |
| Country: Number of subjects enrolled | New Zealand: 7     |
| Worldwide total number of subjects   | 416                |
| EEA total number of subjects         | 104                |

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)                      | 344 |
| From 65 to 84 years                       | 72  |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details:

Participants were enrolled at study sites in North America, Europe, and Asia Pacific. The first participant was screened on 11 November 2015. The last study visit occurred on 21 June 2017.

### Pre-assignment

Screening details:

520 participants were screened.

### Period 1

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

### Arms

|                              |                             |
|------------------------------|-----------------------------|
| Are arms mutually exclusive? | Yes                         |
| <b>Arm title</b>             | SOF/VEL/VOX (Primary Study) |

Arm description:

SOF/VEL/VOX for 12 weeks

|  |   |
|--|---|
| Arm type                               | Experimental                                  |
| Investigational medicinal product name | Sofosbuvir/velpatasvir/voxilaprevir           |
| Investigational medicinal product code |   |
| Other name                             | Vosevi®, GS-7977/GS-5816/GS-9857, SOF/VEL/VOX |
| Pharmaceutical forms                   | Tablet  |
| Routes of administration               | Oral use                                      |

Dosage and administration details:

400/100/100 mg fixed-dose combination (FDC) tablet administered orally once daily with food

|                  |                         |
|------------------|-------------------------|
| <b>Arm title</b> | Placebo (Primary Study) |
|------------------|-------------------------|

Arm description:

Placebo 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:

Tablet administered orally once daily with food

| <b>Number of subjects in period 1<sup>[1]</sup></b> | <b>SOF/VEL/VOX (Primary Study)</b> | <b>Placebo (Primary Study)</b> |
|---|------------------------------------|--------------------------------|
| Started   | 263                                | 152                            |
| Completed   | 257                                | 152                            |
| Not completed                                       | 6                                  | 0                              |
| Withdrew Consent                                    | 2                                  | -                              |
| Lost to follow-up                                   | 4                                  | -                              |

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 in the SOF/VEL/VOX (Primary Study) group who was randomized but never treated is not included in the subject disposition table.

## Period 2

|                              |                             |
|------------------------------|-----------------------------|
| Period 2 title               | Deferred Treatment Substudy |
| Is this the baseline period? | No                          |
| Allocation method            | Not applicable              |
| Blinding used                | Not blinded                 |

## Arms

|                  |   |
|------------------|---|
| <b>Arm title</b> | SOF/VEL/VOX (Deferred Treatment Substudy) |
|------------------|---|

Arm description:

Participants who completed placebo treatment were eligible to enroll in to the open-label Deferred Treatment Substudy to receive SOF/VEL/VOX (400/100/100 mg) FDC tablet orally once daily with food for 12 weeks.

|  |   |
|--|---|
| Arm type                               | Experimental                                  |
| Investigational medicinal product name | Sofosbuvir/velpatasvir/voxilaprevir           |
| Investigational medicinal product code |   |
| Other name                             | Vosevi®, GS-7977/GS-5816/GS-9857, SOF/VEL/VOX |
| Pharmaceutical forms                   | Tablet  |
| Routes of administration               | Oral use                                      |

Dosage and administration details:

400/100/100 mg fixed-dose combination (FDC) tablet administered orally once daily with food

| <b>Number of subjects in period 2<sup>[2]</sup></b> | <b>SOF/VEL/VOX (Deferred Treatment Substudy)</b> |
|---|--|
| Started   | 147  |
| Completed   | 142  |
| Not completed                                       | 5  |
| Withdrew Consent                                    | 1  |
| Lost to follow-up                                   | 4  |

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Only participants who completed placebo treatment and continued to meet the treatment criteria were eligible to enroll in to the open-label Deferred Treatment Substudy.

## Baseline characteristics

### Reporting groups

|                              |                             |
|------------------------------|-----------------------------|
| Reporting group title        | SOF/VEL/VOX (Primary Study) |
| Reporting group description: |                             |
| SOF/VEL/VOX for 12 weeks     |                             |
| Reporting group title        | Placebo (Primary Study)     |
| Reporting group description: |                             |
| Placebo 12 weeks             |                             |

| Reporting group values | SOF/VEL/VOX<br>(Primary Study) | Placebo (Primary<br>Study) | Total |
|------------------------|--------------------------------|----------------------------|-------|
| Number of subjects     | 263                            | 152                        | 415   |
| Age categorical        |                                |                            |       |
| Units: Subjects        |                                |                            |       |

|  |       |       |     |
|--|-------|-------|-----|
| Age continuous   |       |       |     |
| Units: years   |       |       |     |
| arithmetic mean  | 58    | 59    |     |
| standard deviation   | ± 8.5 | ± 8.0 | -   |
| Gender categorical   |       |       |     |
| Units: Subjects  |       |       |     |
| Female   | 63    | 31    | 94  |
| Male   | 200   | 121   | 321 |
| Race   |       |       |     |
| Units: Subjects  |       |       |     |
| White  | 211   | 124   | 335 |
| Black or African American  | 38    | 22    | 60  |
| Asian  | 8     | 6     | 14  |
| Native Hawaiian or Pacific Islander                              | 3     | 0     | 3   |
| Not Disclosed  | 1     | 0     | 1   |
| American Indian or Alaska Native                                 | 1     | 0     | 1   |
| Other  | 1     | 0     | 1   |
| Ethnicity  |       |       |     |
| Units: Subjects  |       |       |     |
| Hispanic or Latino   | 15    | 10    | 25  |
| Not Hispanic or Latino   | 247   | 142   | 389 |
| Not Disclosed  | 1     | 0     | 1   |
| IL28b Status   |       |       |     |
| The CC, CT, and TT alleles are different forms of the IL28b gene |       |       |     |
| Units: Subjects  |       |       |     |
| CC   | 47    | 27    | 74  |
| CT   | 165   | 93    | 258 |
| TT   | 51    | 32    | 83  |
| HCV RNA Category   |       |       |     |
| Units: Subjects  |       |       |     |
| < 800,000 IU/mL  | 73    | 36    | 109 |
| ≥ 800,000 IU/mL  | 190   | 116   | 306 |

|                    |        |        |   |
|--------------------|--------|--------|---|
| HCV RNA            |        |        |   |
| Units: log10 IU/mL |        |        |   |
| arithmetic mean    | 6.3    | 6.3    |   |
| standard deviation | ± 0.68 | ± 0.63 | - |

## End points

### End points reporting groups

|  |   |
|--|---|
| Reporting group title  | SOF/VEL/VOX (Primary Study)               |
| Reporting group description:   |   |
| SOF/VEL/VOX for 12 weeks   |   |
| Reporting group title  | Placebo (Primary Study)                   |
| Reporting group description:   |   |
| Placebo 12 weeks   |   |
| Reporting group title  | SOF/VEL/VOX (Deferred Treatment Substudy) |
| Reporting group description:   |   |
| Participants who completed placebo treatment were eligible to enroll in to the open-label Deferred Treatment Substudy to receive SOF/VEL/VOX (400/100/100 mg) FDC tablet orally once daily with food for 12 weeks. |   |

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

|  |   |
|--|---|
| End point title  | Percentage of Participants With Sustained Virologic Response (SVR) 12 Weeks After Discontinuation of Therapy (SVR12) (Primary Study) <sup>[1]</sup> |
| End point description:   |   |
| SVR12 was defined as HCV RNA < the lower limit of quantitation (LLOQ) at 12 weeks after stopping study treatment. Participants in the Full Analysis Set (all randomized/enrolled participants who took at least 1 dose of study drug) were analyzed. |   |
| 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: The statistical analysis of this primary endpoint is provided in the attachment.  |   |

| End point values                  | SOF/VEL/VOX (Primary Study) | Placebo (Primary Study) |  |  |
|-----------------------------------|-----------------------------|-------------------------|--|--|
| Subject group type                | Reporting group             | Reporting group         |  |  |
| Number of subjects analysed       | 263                         | 152                     |  |  |
| Units: percentage of participants |                             |                         |  |  |
| number (confidence interval 95%)  | 96.2 (93.1 to 98.8)         | 0 (0.0 to 2.4)          |  |  |

|                            |  |
|----------------------------|--|
| Attachments (see zip file) | 367-1171_PrimaryEndpoint_StatsAnalysis.pdf |
|----------------------------|--|

### Statistical analyses

No statistical analyses for this end point

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



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

End point description:

Participants in the Full Analysis Set (all randomized/enrolled participants who took at least 1 dose of study drug) were analyzed.

|                |         |
|----------------|---------|
| 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>(Primary Study) | Placebo<br>(Primary Study) |  |  |
|-----------------------------------|--------------------------------|----------------------------|--|--|
| Subject group type                | Reporting group                | Reporting group            |  |  |
| Number of subjects analysed       | 263                            | 152                        |  |  |
| Units: percentage of participants |                                |                            |  |  |
| number (not applicable)           | 0.4                            | 2.0                        |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With SVR at 4 Weeks After Discontinuation of Therapy (SVR4) (Primary Study)

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants With SVR at 4 Weeks After Discontinuation of Therapy (SVR4) (Primary Study) |
|-----------------|--|

End point description:

SVR4 was defined as HCV RNA < LLOQ at 4 weeks after stopping study treatment, respectively. Participants in the Full Analysis Set (all randomized/enrolled participants who took at least 1 dose of study drug) were analyzed.

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

End point timeframe:

Posttreatment Week 4

| End point values                  | SOF/VEL/VOX<br>(Primary Study) | Placebo<br>(Primary Study) |  |  |
|-----------------------------------|--------------------------------|----------------------------|--|--|
| Subject group type                | Reporting group                | Reporting group            |  |  |
| Number of subjects analysed       | 263                            | 152                        |  |  |
| Units: percentage of participants |                                |                            |  |  |
| number (confidence interval 95%)  | 97.7 (95.1 to 99.2)            | 0 (0.0 to 2.4)             |  |  |

## Statistical analyses

No statistical analyses for this end point

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**Secondary: Percentage of Participants With HCV RNA < LLOQ On Treatment (Primary Study)**

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|                 |   |
|-----------------|---|
| End point title | Percentage of Participants With HCV RNA < LLOQ On Treatment (Primary Study) |
|-----------------|---|

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, 8 and 12

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| End point values                                    | SOF/VEL/VOX<br>(Primary<br>Study) | Placebo<br>(Primary<br>Study) |  |  |
|---|-----------------------------------|-------------------------------|--|--|
| Subject group type                                  | Reporting group                   | Reporting group               |  |  |
| Number of subjects analysed                         | 263                               | 152                           |  |  |
| Units: percentage of participants                   |                                   |                               |  |  |
| number (confidence interval 95%)                    |                                   |                               |  |  |
| Week 1 (SOF/VEL/VOX: N = 263;<br>Placebo: N = 152)  | 15.6 (11.4 to<br>20.5)            | 0 (0.0 to 2.4)                |  |  |
| Week 2 (SOF/VEL/VOX: N = 263;<br>Placebo: N = 150)  | 56.7 (50.4 to<br>62.7)            | 0 (0.0 to 2.4)                |  |  |
| Week 4 (SOF/VEL/VOX: N = 262;<br>Placebo: N = 150)  | 92.7 (88.9 to<br>95.6)            | 0 (0.0 to 2.4)                |  |  |
| Week 8 (SOF/VEL/VOX: N = 262;<br>Placebo: N = 150)  | 100.0 (98.6 to<br>100.0)          | 0 (0.0 to 2.4)                |  |  |
| Week 12 (SOF/VEL/VOX: N = 261;<br>Placebo: N = 149) | 99.6 (97.9 to<br>100.0)           | 0 (0.0 to 2.4)                |  |  |

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Change From Baseline in HCV RNA (Primary Study)**

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|                 |   |
|-----------------|---|
| End point title | Change From Baseline in HCV RNA (Primary Study) |
|-----------------|---|

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, 8 and 12

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| End point values                                    | SOF/VEL/VOX<br>(Primary Study) | Placebo<br>(Primary Study) |  |  |
|---|--------------------------------|----------------------------|--|--|
| Subject group type                                  | Reporting group                | Reporting group            |  |  |
| Number of subjects analysed                         | 262                            | 150                        |  |  |
| Units: log10 IU/mL                                  |                                |                            |  |  |
| arithmetic mean (standard deviation)                |                                |                            |  |  |
| Week 1 (SOF/VEL/VOX: N = 258;<br>Placebo: N = 150)  | -4.20 (± 0.733)                | 0.02 (± 0.300)             |  |  |
| Week 2 (SOF/VEL/VOX: N = 261;<br>Placebo: N = 148)  | -4.81 (± 0.704)                | 0.02 (± 0.322)             |  |  |
| Week 4 (SOF/VEL/VOX: N = 261;<br>Placebo: N = 150)  | -5.07 (± 0.677)                | -0.01 (± 0.441)            |  |  |
| Week 8 (SOF/VEL/VOX: N = 262;<br>Placebo: N = 149)  | -5.11 (± 0.678)                | 0.05 (± 0.434)             |  |  |
| Week 12 (SOF/VEL/VOX: N = 261;<br>Placebo: N = 138) | -5.10 (± 0.690)                | 0.03 (± 0.430)             |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants With SVR at 24 Weeks After Discontinuation of Therapy (SVR24) (Primary Study)

|                        |  |
|------------------------|--|
| End point title        | Percentage of Participants With SVR at 24 Weeks After Discontinuation of Therapy (SVR24) (Primary Study) <sup>[3]</sup>              |
| End point description: | SVR24 was defined as HCV RNA < LLOQ at 24 weeks after stopping study treatment. Participants in the Full Analysis Set were analyzed. |
| End point type         | Secondary  |
| End point timeframe:   |  |
| Posttreatment Week 24  |  |

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.  
Justification: SVR24 was not assessed for the placebo group.

| End point values                  | SOF/VEL/VOX<br>(Primary Study) |  |  |  |
|-----------------------------------|--------------------------------|--|--|--|
| Subject group type                | Reporting group                |  |  |  |
| Number of subjects analysed       | 263                            |  |  |  |
| Units: percentage of participants |                                |  |  |  |
| number (confidence interval 95%)  | 96.2 (93.1 to 98.2)            |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants With Virologic Failure (Primary Study)

|   |  |
|---|--|
| End point title   | Percentage of Participants With Virologic Failure (Primary Study) <sup>[4]</sup> |
| End point description:  |  |
| Virologic failure is defined as:  |  |
| <ul style="list-style-type: none"> <li>• On-treatment virologic failure:</li> <li>• Breakthrough (confirmed HCV RNA <math>\geq</math> LLOQ after having previously had HCV RNA LLOQ while on treatment),</li> </ul>   |  |
| or  |  |
| <ul style="list-style-type: none"> <li>• Rebound (confirmed 1 log<sub>10</sub> IU/mL increase in HCV RNA from nadir while on treatment), or</li> <li>• Non-response (HCV RNA persistently <math>\geq</math> LLOQ through 8 weeks of treatment)</li> <li>• Virologic relapse:</li> <li>• Confirmed HCV RNA <math>\geq</math> LLOQ during the posttreatment period having achieved HCV RNA LLOQ at last ontreatment visit.</li> </ul> |  |
| Participants in the Full Analysis Set were analyzed.  |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| Up to Posttreatment Week 24   |  |

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.  
Justification: Virological failure was not assessed for the placebo group.

|                                   |                                |  |  |  |
|-----------------------------------|--------------------------------|--|--|--|
| <b>End point values</b>           | SOF/VEL/VOX<br>(Primary Study) |  |  |  |
| Subject group type                | Reporting group                |  |  |  |
| Number of subjects analysed       | 263                            |  |  |  |
| Units: percentage of participants |                                |  |  |  |
| number (not applicable)           | 2.7                            |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants With SVR at 4, 12, and 24 Weeks After Discontinuation of Therapy (Deferred Treatment Substudy)

|   |   |
|---|---|
| End point title   | Percentage of Participants With SVR at 4, 12, and 24 Weeks After Discontinuation of Therapy (Deferred Treatment Substudy) |
| End point description:  |   |
| SVR4, SVR12 and SVR24 was defined as HCV RNA < LLOQ at 4, 12 and 24 weeks after stopping study treatment respectively. Participants in the Full Analysis Set (all enrolled participants who took at least 1 dose of study drug) from the Deferred Treatment Substudy were analyzed. |   |
| End point type  | Secondary   |
| End point timeframe:  |   |
| Posttreatment Weeks 4, 12, and 24 (Deferred Treatment Substudy)   |   |

|                                   |  |  |  |  |
|-----------------------------------|--|--|--|--|
| <b>End point values</b>           | SOF/VEL/VOX<br>(Deferred<br>Treatment<br>Substudy) |  |  |  |
| Subject group type                | Reporting group                                    |  |  |  |
| Number of subjects analysed       | 147  |  |  |  |
| Units: percentage of participants |  |  |  |  |
| number (confidence interval 95%)  |  |  |  |  |
| SVR4                              | 98.6 (95.2 to<br>99.8)                             |  |  |  |
| SVR12                             | 97.3 (93.2 to<br>99.3)                             |  |  |  |
| SVR24                             | 97.3 (93.2 to<br>99.3)                             |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants With HCV RNA < LLOQ On Treatment (Deferred Treatment Substudy)

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants With HCV RNA < LLOQ On Treatment (Deferred Treatment Substudy) |
|-----------------|---|

End point description:

Participants in the Full Analysis Set of the Deferred Treatment Substudy were analyzed.

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

End point timeframe:

Weeks 1, 2, 4, 8 and 12 (Deferred Treatment Substudy)

|                                   |  |  |  |  |
|-----------------------------------|--|--|--|--|
| <b>End point values</b>           | SOF/VEL/VOX<br>(Deferred<br>Treatment<br>Substudy) |  |  |  |
| Subject group type                | Reporting group                                    |  |  |  |
| Number of subjects analysed       | 147  |  |  |  |
| Units: percentage of participants |  |  |  |  |
| number (confidence interval 95%)  |  |  |  |  |
| Week 1                            | 14.3 (9.1 to<br>21.0)                              |  |  |  |
| Week 2                            | 62.6 (54.2 to<br>70.4)                             |  |  |  |
| Week 4                            | 93.2 (87.8 to<br>96.7)                             |  |  |  |
| Week 8                            | 100.0 (97.5 to<br>100.0)                           |  |  |  |
| Week 12                           | 100.0 (97.5 to<br>100.0)                           |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in HCV RNA (Deferred Treatment Substudy)

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in HCV RNA (Deferred Treatment Substudy) |
|-----------------|---|

End point description:

Participants with available data in the Full Analysis Set of the Deferred Treatment Substudy were analyzed.

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

End point timeframe:

Baseline; Weeks 1, 2, 4, 8, and 12 (Deferred Treatment Substudy)

| End point values                     | SOF/VEL/VOX<br>(Deferred<br>Treatment<br>Substudy) |  |  |  |
|--------------------------------------|--|--|--|--|
| Subject group type                   | Reporting group                                    |  |  |  |
| Number of subjects analysed          | 147  |  |  |  |
| Units: log10 IU/mL                   |  |  |  |  |
| arithmetic mean (standard deviation) |  |  |  |  |
| Week 1 (N = 139)                     | -4.30 (±<br>0.626)                                 |  |  |  |
| Week 2 (N = 145)                     | -4.93 (±<br>0.602)                                 |  |  |  |
| Week 4 (N = 147)                     | -5.16 (±<br>0.512)                                 |  |  |  |
| Week 8 (N=147)                       | -5.20 (±<br>0.532)                                 |  |  |  |
| Week 12 (N= 147)                     | -5.20 (±<br>0.532)                                 |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants With Virologic Failure (Deferred Treatment Substudy)

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants With Virologic Failure (Deferred Treatment Substudy) |
|-----------------|---|

End point description:

Participants in the Full Analysis Set of the Deferred Treatment Substudy were analyzed.

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

End point timeframe:

Up to Posttreatment Week 24 (Deferred Treatment Substudy)

|                                   |  |  |  |  |
|-----------------------------------|--|--|--|--|
| <b>End point values</b>           | SOF/VEL/VOX<br>(Deferred<br>Treatment<br>Substudy) |  |  |  |
| Subject group type                | Reporting group                                    |  |  |  |
| Number of subjects analysed       | 147  |  |  |  |
| Units: percentage of participants |  |  |  |  |
| number (not applicable)           | 2.7  |  |  |  |

### Statistical analyses

---

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Primary Study: Up to 12 Weeks + 30 days; Deferred Treatment Substudy: Up to 12 Weeks + 30 days

Adverse event reporting additional description:

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

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 20.0 |
|--------------------|------|

### Reporting groups

|                       |                             |
|-----------------------|-----------------------------|
| Reporting group title | SOF/VEL/VOX (Primary Study) |
|-----------------------|-----------------------------|

Reporting group description:

SOF/VEL/VOX (400/100/100 mg) FDC tablet orally once daily with food for 12 weeks

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | Placebo (Primary Study) |
|-----------------------|-------------------------|

Reporting group description:

Placebo tablet orally once daily with food for 12 weeks

|                       |   |
|-----------------------|---|
| Reporting group title | SOF/VEL/VOX (Deferred Treatment Substudy) |
|-----------------------|---|

Reporting group description:

Participants who completed placebo treatment were eligible for open-label Deferred Treatment Substudy.

SOF/VEL/VOX (400/100/100 mg) FDC tablet orally once daily with food for 12 weeks

| Serious adverse events  | SOF/VEL/VOX<br>(Primary Study) | Placebo (Primary<br>Study) | SOF/VEL/VOX<br>(Deferred Treatment<br>Substudy) |
|---|--------------------------------|----------------------------|---|
| Total subjects affected by serious adverse events                   |                                |                            |   |
| subjects affected / exposed   | 5 / 263 (1.90%)                | 7 / 152 (4.61%)            | 6 / 147 (4.08%)                                 |
| 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) |                                |                            |   |
| Adrenal neoplasm  |                                |                            |   |
| subjects affected / exposed   | 1 / 263 (0.38%)                | 0 / 152 (0.00%)            | 0 / 147 (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   |
| Basal cell carcinoma  |                                |                            |   |
| subjects affected / exposed   | 0 / 263 (0.00%)                | 1 / 152 (0.66%)            | 0 / 147 (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   |
| Ovarian cancer  |                                |                            |   |



|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 263 (0.38%) | 0 / 152 (0.00%) | 0 / 147 (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           |
| Injury, poisoning and procedural complications  |                 |                 |                 |
| Subdural haematoma                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 263 (0.00%) | 1 / 152 (0.66%) | 0 / 147 (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           |
| Wrist fracture                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 263 (0.00%) | 0 / 152 (0.00%) | 1 / 147 (0.68%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Vascular disorders                              |                 |                 |                 |
| Arteritis                                       |                 |                 |                 |
| subjects affected / exposed                     | 1 / 263 (0.38%) | 0 / 152 (0.00%) | 0 / 147 (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           |
| Cardiac disorders                               |                 |                 |                 |
| Acute myocardial infarction                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 263 (0.00%) | 0 / 152 (0.00%) | 1 / 147 (0.68%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Atrial fibrillation                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 263 (0.00%) | 1 / 152 (0.66%) | 0 / 147 (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           |
| Ventricular fibrillation                        |                 |                 |                 |
| subjects affected / exposed                     | 0 / 263 (0.00%) | 1 / 152 (0.66%) | 0 / 147 (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           |
| Nervous system disorders                        |                 |                 |                 |
| Cerebral haemorrhage                            |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 263 (0.38%) | 0 / 152 (0.00%) | 0 / 147 (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           |
| Generalised tonic-clonic seizure                |                 |                 |                 |
| subjects affected / exposed                     | 0 / 263 (0.00%) | 0 / 152 (0.00%) | 1 / 147 (0.68%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Seizure   |                 |                 |                 |
| subjects affected / exposed                     | 1 / 263 (0.38%) | 0 / 152 (0.00%) | 0 / 147 (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           |
| Gastrointestinal disorders                      |                 |                 |                 |
| Mesenteric vein thrombosis                      |                 |                 |                 |
| subjects affected / exposed                     | 0 / 263 (0.00%) | 0 / 152 (0.00%) | 1 / 147 (0.68%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hepatobiliary disorders                         |                 |                 |                 |
| Hepatic failure                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 263 (0.00%) | 1 / 152 (0.66%) | 0 / 147 (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           |
| Respiratory, thoracic and mediastinal disorders |                 |                 |                 |
| Chronic obstructive pulmonary disease           |                 |                 |                 |
| subjects affected / exposed                     | 1 / 263 (0.38%) | 0 / 152 (0.00%) | 0 / 147 (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           |
| Psychiatric disorders                           |                 |                 |                 |
| Schizophrenia                                   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 263 (0.00%) | 1 / 152 (0.66%) | 0 / 147 (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           |
| Renal and urinary disorders                     |                 |                 |                 |
| Nephrolithiasis                                 |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 263 (0.00%) | 0 / 152 (0.00%) | 1 / 147 (0.68%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Infections and infestations</b>              |                 |                 |                 |
| Pneumonia                                       |                 |                 |                 |
| subjects affected / exposed                     | 1 / 263 (0.38%) | 0 / 152 (0.00%) | 0 / 147 (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           |
| Scrotal infection                               |                 |                 |                 |
| subjects affected / exposed                     | 0 / 263 (0.00%) | 1 / 152 (0.66%) | 0 / 147 (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           |
| Urosepsis                                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 263 (0.00%) | 0 / 152 (0.00%) | 1 / 147 (0.68%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

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

| <b>Non-serious adverse events</b>                           | SOF/VEL/VOX<br>(Primary Study) | Placebo (Primary<br>Study) | SOF/VEL/VOX<br>(Deferred Treatment<br>Substudy) |
|---|--------------------------------|----------------------------|---|
| Total subjects affected by non-serious adverse events       |                                |                            |   |
| subjects affected / exposed                                 | 206 / 263 (78.33%)             | 107 / 152 (70.39%)         | 87 / 147 (59.18%)                               |
| <b>Nervous system disorders</b>                             |                                |                            |   |
| Headache  |                                |                            |   |
| subjects affected / exposed                                 | 66 / 263 (25.10%)              | 26 / 152 (17.11%)          | 29 / 147 (19.73%)                               |
| occurrences (all)   | 72                             | 32                         | 30  |
| Dizziness   |                                |                            |   |
| subjects affected / exposed                                 | 11 / 263 (4.18%)               | 14 / 152 (9.21%)           | 7 / 147 (4.76%)                                 |
| occurrences (all)   | 11                             | 14                         | 7   |
| <b>General disorders and administration site conditions</b> |                                |                            |   |
| Fatigue   |                                |                            |   |
| subjects affected / exposed                                 | 56 / 263 (21.29%)              | 30 / 152 (19.74%)          | 31 / 147 (21.09%)                               |
| occurrences (all)   | 58                             | 30                         | 31  |
| Asthenia  |                                |                            |   |

|  |                        |                      |                      |
|--|------------------------|----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all) | 20 / 263 (7.60%)<br>22 | 9 / 152 (5.92%)<br>9 | 3 / 147 (2.04%)<br>3 |
| Gastrointestinal disorders                       |                        |                      |                      |
| Diarrhoea  |                        |                      |                      |
| subjects affected / exposed                      | 48 / 263 (18.25%)      | 19 / 152 (12.50%)    | 28 / 147 (19.05%)    |
| occurrences (all)                                | 58                     | 24                   | 32                   |
| Nausea   |                        |                      |                      |
| subjects affected / exposed                      | 37 / 263 (14.07%)      | 12 / 152 (7.89%)     | 21 / 147 (14.29%)    |
| occurrences (all)                                | 41                     | 13                   | 24                   |
| Psychiatric disorders                            |                        |                      |                      |
| Insomnia   |                        |                      |                      |
| subjects affected / exposed                      | 19 / 263 (7.22%)       | 8 / 152 (5.26%)      | 5 / 147 (3.40%)      |
| occurrences (all)                                | 19                     | 8                    | 5                    |
| Musculoskeletal and connective tissue disorders  |                        |                      |                      |
| Back pain  |                        |                      |                      |
| subjects affected / exposed                      | 11 / 263 (4.18%)       | 8 / 152 (5.26%)      | 7 / 147 (4.76%)      |
| occurrences (all)                                | 11                     | 8                    | 7                    |
| Arthralgia                                       |                        |                      |                      |
| subjects affected / exposed                      | 8 / 263 (3.04%)        | 8 / 152 (5.26%)      | 9 / 147 (6.12%)      |
| occurrences (all)                                | 8                      | 8                    | 10                   |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment   |
|-----------------|---|
| 09 October 2015 | <ul style="list-style-type: none"><li>• The definition of treatment experience for eligibility has been revised from DAA-experienced to NS5A inhibitor-experienced.</li><li>• Participants with DAA experience that did not include an NS5A inhibitor will be eligible for screening in a separate protocol Study GS-US-367-1170.</li><li>• The total number of study centers participating has been increased from 100 to 120.</li><li>• Revisions have been made to the approximate number of participants by genotype to be randomized or enrolled into each group</li><li>• The randomization ratio for Group 1 subjects with genotype 1 has been revised from 2:1 to 1:1</li><li>• Updates have been made to Section 1 including 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>• Section 6 Procedures has been revised to now include procedures for breaking treatment code/unblinding of subjects for medical emergencies.</li><li>• Additional formatting, minor grammatical corrections and updates were made throughout the document.</li></ul> |

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/28564569>