



## Clinical trial results:

### Open-Label Study to Evaluate the Safety and Efficacy of Ledipasvir/Sofosbuvir (LDV/SOF) Fixed-Dose Combination (FDC) for 6 Weeks in Subjects with Acute Genotype 1 or 4 Hepatitis C Virus (HCV) and Chronic Human Immunodeficiency Virus (HIV)-1 Co-Infection

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2014-004812-12  |
| Trial protocol           | DE GB           |
| Global end of trial date | 08 January 2016 |

#### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 23 January 2017 |
| First version publication date | 23 January 2017 |

#### Trial information

##### Trial identification

|                       |                |
|-----------------------|----------------|
| Sponsor protocol code | GS-US-337-1612 |
|-----------------------|----------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02457611 |
| 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                       | 08 January 2016 |
| Is this the analysis of the primary completion data? | No              |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 08 January 2016 |
| 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 determine the antiviral efficacy, safety, and tolerability of ledipasvir/sofosbuvir (LDV/SOF) fixed-dose combination (FDC) in adults with acute genotype 1 or 4 hepatitis C virus (HCV) and chronic human immunodeficiency virus (HIV)-1 co-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                          | 11 June 2015 |
| Long term follow-up planned                               | No           |
| Independent data monitoring committee (IDMC) involvement? | No           |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United Kingdom: 11 |
| Country: Number of subjects enrolled | Germany: 15        |
| Worldwide total number of subjects   | 26                 |
| EEA total number of subjects         | 26                 |

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)      | 26 |
| From 65 to 84 years       | 0  |
| 85 years and over         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Participants were enrolled at study sites in Germany and the United Kingdom. The first participant was screened on 11 June 2015. The last study visit occurred on 8 January 2016.

### Pre-assignment

Screening details:

34 participants were screened.

### Period 1

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

### Arms

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

Arm description:

Ledipasvir/sofosbuvir (Harvoni®; LDV/SOF) (90/400 mg) fixed-dose combination (FDC) tablet administered once daily for 6 weeks

|                                        |                           |
|----------------------------------------|---------------------------|
| Arm type                               | Experimental              |
| Investigational medicinal product name | Ledipasvir/sofosbuvir     |
| Investigational medicinal product code |                           |
| Other name                             | Harvoni®; GS-5885/GS-7977 |
| Pharmaceutical forms                   | Tablet                    |
| Routes of administration               | Oral use                  |

Dosage and administration details:

90/400 mg FDC administered once daily

| Number of subjects in period 1 | LDV/SOF |
|--------------------------------|---------|
| Started                        | 26      |
| Completed                      | 23      |
| Not completed                  | 3       |
| Lost to follow-up              | 3       |

## Baseline characteristics

### Reporting groups

|                                                                                                                               |         |
|-------------------------------------------------------------------------------------------------------------------------------|---------|
| Reporting group title                                                                                                         | LDV/SOF |
| Reporting group description:                                                                                                  |         |
| Ledipasvir/sofosbuvir (Harvoni®; LDV/SOF) (90/400 mg) fixed-dose combination (FDC) tablet administered once daily for 6 weeks |         |

| Reporting group values    | LDV/SOF | Total |  |
|---------------------------|---------|-------|--|
| Number of subjects        | 26      | 26    |  |
| Age categorical           |         |       |  |
| Units: Subjects           |         |       |  |
| Age continuous            |         |       |  |
| Units: years              |         |       |  |
| arithmetic mean           | 41      |       |  |
| standard deviation        | ± 8.8   | -     |  |
| Gender categorical        |         |       |  |
| Units: Subjects           |         |       |  |
| Female                    | 0       | 0     |  |
| Male                      | 26      | 26    |  |
| Race                      |         |       |  |
| Units: Subjects           |         |       |  |
| Black or African American | 1       | 1     |  |
| White                     | 24      | 24    |  |
| Asian                     | 1       | 1     |  |
| Ethnicity                 |         |       |  |
| Units: Subjects           |         |       |  |
| Hispanic or Latino        | 1       | 1     |  |
| Not Hispanic or Latino    | 22      | 22    |  |
| Not Disclosed             | 3       | 3     |  |
| IL28b Status              |         |       |  |
| Units: Subjects           |         |       |  |
| CC                        | 12      | 12    |  |
| CT                        | 11      | 11    |  |
| TT                        | 3       | 3     |  |
| HCV Genotype              |         |       |  |
| Units: Subjects           |         |       |  |
| Genotype 1a               | 19      | 19    |  |
| Genotype 4                | 7       | 7     |  |
| HCV RNA Category          |         |       |  |
| Units: Subjects           |         |       |  |
| < 800,000 IU/mL           | 14      | 14    |  |
| ≥ 800,000 IU/mL           | 12      | 12    |  |
| HCV RNA                   |         |       |  |
| Units: log10 IU/mL        |         |       |  |
| arithmetic mean           | 5.4     |       |  |
| standard deviation        | ± 1.6   | -     |  |
| CD4 Counts                |         |       |  |

|                    |         |   |  |
|--------------------|---------|---|--|
| Units: cells/uL    |         |   |  |
| arithmetic mean    | 675     |   |  |
| standard deviation | ± 251.3 | - |  |

## End points

### End points reporting groups

|                                                                                                                                                               |         |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|
| Reporting group title                                                                                                                                         | LDV/SOF |
| Reporting group description:<br>Ledipasvir/sofosbuvir (Harvoni®; LDV/SOF) (90/400 mg) fixed-dose combination (FDC) tablet administered once daily for 6 weeks |         |

### Primary: Percentage of Participants With Sustained Virologic Response 12 Weeks After Completion of Treatment (SVR12)

|                 |                                                                                                                            |
|-----------------|----------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of Participants With Sustained Virologic Response 12 Weeks After Completion of Treatment (SVR12) <sup>[1]</sup> |
|-----------------|----------------------------------------------------------------------------------------------------------------------------|

End point description:

SVR12 was defined as HCV RNA < the lower limit of quantitation (LLOQ) 12 weeks following the last dose of study drug.

Full Analysis Set: participants with genotype 1 or 4 HCV infection who were 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: No statistical comparison was planned or performed.

| End point values                  | LDV/SOF           |  |  |  |
|-----------------------------------|-------------------|--|--|--|
| Subject group type                | Reporting group   |  |  |  |
| Number of subjects analysed       | 26                |  |  |  |
| Units: Percentage of participants |                   |  |  |  |
| number (confidence interval 95%)  | 76.9 (56.4 to 91) |  |  |  |

### 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 <sup>[2]</sup> |
|-----------------|---------------------------------------------------------------------------------------------------------------|

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 6 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.

|                                   |                 |  |  |  |
|-----------------------------------|-----------------|--|--|--|
| <b>End point values</b>           | LDV/SOF         |  |  |  |
| Subject group type                | Reporting group |  |  |  |
| Number of subjects analysed       | 26              |  |  |  |
| Units: Percentage of participants |                 |  |  |  |
| number (not applicable)           | 0               |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants With Sustained Virologic Response 4 Weeks After Discontinuation of Study Treatment (SVR4)

|                 |                                                                                                                      |
|-----------------|----------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of Participants With Sustained Virologic Response 4 Weeks After Discontinuation of Study Treatment (SVR4) |
|-----------------|----------------------------------------------------------------------------------------------------------------------|

End point description:

SVR4 was defined as HCV RNA < LLOQ 4 weeks after the last dose of study drug.

Full Analysis Set

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

End point timeframe:

Posttreatment Week 4

|                                   |                     |  |  |  |
|-----------------------------------|---------------------|--|--|--|
| <b>End point values</b>           | LDV/SOF             |  |  |  |
| Subject group type                | Reporting group     |  |  |  |
| Number of subjects analysed       | 26                  |  |  |  |
| Units: Percentage of Participants |                     |  |  |  |
| number (confidence interval 95%)  | 84.6 (65.1 to 95.6) |  |  |  |

### 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:

Full Analysis Set

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

End point timeframe:

Weeks 2, 4, and 6

| End point values                  | LDV/SOF             |  |  |  |
|-----------------------------------|---------------------|--|--|--|
| Subject group type                | Reporting group     |  |  |  |
| Number of subjects analysed       | 26                  |  |  |  |
| Units: Percentage of Participants |                     |  |  |  |
| number (confidence interval 95%)  |                     |  |  |  |
| Week 2                            | 73.1 (52.2 to 88.4) |  |  |  |
| Week 4                            | 88.5 (69.8 to 97.6) |  |  |  |
| Week 6                            | 96.2 (80.4 to 99.9) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in HCV RNA at Weeks 2, 4, and 6

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

| End point values                     | LDV/SOF         |  |  |  |
|--------------------------------------|-----------------|--|--|--|
| Subject group type                   | Reporting group |  |  |  |
| Number of subjects analysed          | 26              |  |  |  |
| Units: log10 IU/mL                   |                 |  |  |  |
| arithmetic mean (standard deviation) |                 |  |  |  |
| Change at Week 2 (N=26)              | -4.01 (± 1.497) |  |  |  |
| Change at Week 4 (N= 25)             | -4.16 (± 1.583) |  |  |  |
| Change at Week 6 (N= 25)             | -4.17 (± 1.583) |  |  |  |

### 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:                                                                                                                                                         |                                                   |
| On-treatment virologic failure                                                                                                                                                            |                                                   |
| confirmed HCV RNA $\geq$ LLOQ after having previously had HCV RNA $<$ LLOQ, while on treatment (ie, breakthrough),                                                                        |                                                   |
| confirmed $> 1$ log <sub>10</sub> IU/mL increase in HCV RNA from nadir while on treatment (ie, rebound),                                                                                  |                                                   |
| HCV RNA persistently $\geq$ LLOQ through end of treatment (ie, nonresponse)                                                                                                               |                                                   |
| Relapse                                                                                                                                                                                   |                                                   |
| HCV RNA $\geq$ LLOQ during the posttreatment period having achieved HCV RNA $<$ LLOQ at end of treatment, confirmed with 2 consecutive values or last available posttreatment measurement |                                                   |
| End point type                                                                                                                                                                            | Secondary                                         |
| End point timeframe:                                                                                                                                                                      |                                                   |
| Up to Posttreatment Week 12                                                                                                                                                               |                                                   |

|                                   |                 |  |  |  |
|-----------------------------------|-----------------|--|--|--|
| <b>End point values</b>           | LDV/SOF         |  |  |  |
| Subject group type                | Reporting group |  |  |  |
| Number of subjects analysed       | 26              |  |  |  |
| Units: Percentage of participants |                 |  |  |  |
| number (not applicable)           | 15.4            |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in HIV RNA From Day 1 to End of Treatment as Assessed by Proportion of Participants Who Had Confirmed HIV Virologic Rebound During the Study.

|                                                                                                                                                                                                                  |                                                                                                                                                      |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                  | Change in HIV RNA From Day 1 to End of Treatment as Assessed by Proportion of Participants Who Had Confirmed HIV Virologic Rebound During the Study. |
| End point description:                                                                                                                                                                                           |                                                                                                                                                      |
| Participants with HIV virologic rebound was defined as participants with at least two HIV RNA $\geq 400$ copies/mL at 2 consecutive post-baseline visits which are at least 2 weeks apart based on actual dates. |                                                                                                                                                      |
| Safety Analysis Set                                                                                                                                                                                              |                                                                                                                                                      |
| End point type                                                                                                                                                                                                   | Secondary                                                                                                                                            |
| End point timeframe:                                                                                                                                                                                             |                                                                                                                                                      |
| Day 1; Week 6                                                                                                                                                                                                    |                                                                                                                                                      |

|                                |                 |  |  |  |
|--------------------------------|-----------------|--|--|--|
| <b>End point values</b>        | LDV/SOF         |  |  |  |
| Subject group type             | Reporting group |  |  |  |
| Number of subjects analysed    | 26              |  |  |  |
| Units: log <sub>10</sub> IU/mL |                 |  |  |  |
| number (not applicable)        | 0               |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants That Maintain HIV-1 RNA < 50 Copies/mL While on HCV Treatment and at Posttreatment Week 4

|                 |                                                                                                                      |
|-----------------|----------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of Participants That Maintain HIV-1 RNA < 50 Copies/mL While on HCV Treatment and at Posttreatment Week 4 |
|-----------------|----------------------------------------------------------------------------------------------------------------------|

End point description:

Participants in the Safety Analysis Set who had HIV-1 RNA < 50 copies/mL at Baseline were analyzed.

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

End point timeframe:

Weeks 2, 4, 6, and Posttreatment Week 4

| End point values                  | LDV/SOF             |  |  |  |
|-----------------------------------|---------------------|--|--|--|
| Subject group type                | Reporting group     |  |  |  |
| Number of subjects analysed       | 21                  |  |  |  |
| Units: Percentage of participants |                     |  |  |  |
| number (confidence interval 95%)  |                     |  |  |  |
| Week 2                            | 100 (83.9 to 100)   |  |  |  |
| Week 4                            | 100 (83.9 to 100)   |  |  |  |
| Week 6                            | 95.2 (76.2 to 99.9) |  |  |  |
| Posttreatment Week 4              | 100 (83.9 to 100)   |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percent Change From Baseline on CD4 T-cell Count at the End of Treatment and at Posttreatment Week 4

|                 |                                                                                                      |
|-----------------|------------------------------------------------------------------------------------------------------|
| End point title | Percent Change From Baseline on CD4 T-cell Count at the End of Treatment and at Posttreatment Week 4 |
|-----------------|------------------------------------------------------------------------------------------------------|

End point description:

Participants in the Safety Analysis Set with available data were analyzed.

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

End point timeframe:

Baseline; Week 6; Posttreatment Week 4

|                                         |                 |  |  |  |
|-----------------------------------------|-----------------|--|--|--|
| <b>End point values</b>                 | LDV/SOF         |  |  |  |
| Subject group type                      | Reporting group |  |  |  |
| Number of subjects analysed             | 26              |  |  |  |
| Units: Percent change                   |                 |  |  |  |
| arithmetic mean (standard deviation)    |                 |  |  |  |
| Change at Week 6 (N = 24)               | -0.3 (± 4.91)   |  |  |  |
| Change at Posttreatment Week 4 (N = 23) | 0.4 (± 4.08)    |  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 6 weeks plus 30 days

Adverse event reporting additional description:

Safety Analysis Set

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 18.1 |
|--------------------|------|

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | LDV/SOF |
|-----------------------|---------|

Reporting group description:

LDV/SOF 90/400 mg FDC tablet administered once daily for 6 weeks

| Serious adverse events                               | LDV/SOF        |  |  |
|------------------------------------------------------|----------------|--|--|
| Total subjects affected by serious adverse events    |                |  |  |
| subjects affected / exposed                          | 1 / 26 (3.85%) |  |  |
| number of deaths (all causes)                        | 0              |  |  |
| number of deaths resulting from adverse events       | 0              |  |  |
| Vascular disorders                                   |                |  |  |
| Thrombophlebitis                                     |                |  |  |
| subjects affected / exposed                          | 1 / 26 (3.85%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Nervous system disorders                             |                |  |  |
| Loss of consciousness                                |                |  |  |
| subjects affected / exposed                          | 1 / 26 (3.85%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| General disorders and administration site conditions |                |  |  |
| Pyrexia                                              |                |  |  |
| subjects affected / exposed                          | 1 / 26 (3.85%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Respiratory, thoracic and mediastinal disorders      |                |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| Pneumonia aspiration                            |                |  |  |
| subjects affected / exposed                     | 1 / 26 (3.85%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

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

| <b>Non-serious adverse events</b>                     | LDV/SOF          |  |  |
|-------------------------------------------------------|------------------|--|--|
| Total subjects affected by non-serious adverse events |                  |  |  |
| subjects affected / exposed                           | 20 / 26 (76.92%) |  |  |
| Nervous system disorders                              |                  |  |  |
| Headache                                              |                  |  |  |
| subjects affected / exposed                           | 6 / 26 (23.08%)  |  |  |
| occurrences (all)                                     | 8                |  |  |
| General disorders and administration site conditions  |                  |  |  |
| Fatigue                                               |                  |  |  |
| subjects affected / exposed                           | 7 / 26 (26.92%)  |  |  |
| occurrences (all)                                     | 9                |  |  |
| Gastrointestinal disorders                            |                  |  |  |
| Diarrhoea                                             |                  |  |  |
| subjects affected / exposed                           | 3 / 26 (11.54%)  |  |  |
| occurrences (all)                                     | 4                |  |  |
| Nausea                                                |                  |  |  |
| subjects affected / exposed                           | 3 / 26 (11.54%)  |  |  |
| occurrences (all)                                     | 3                |  |  |
| Toothache                                             |                  |  |  |
| subjects affected / exposed                           | 2 / 26 (7.69%)   |  |  |
| occurrences (all)                                     | 2                |  |  |
| Psychiatric disorders                                 |                  |  |  |
| Insomnia                                              |                  |  |  |
| subjects affected / exposed                           | 3 / 26 (11.54%)  |  |  |
| occurrences (all)                                     | 3                |  |  |
| Infections and infestations                           |                  |  |  |
| Nasopharyngitis                                       |                  |  |  |
| subjects affected / exposed                           | 7 / 26 (26.92%)  |  |  |
| occurrences (all)                                     | 7                |  |  |
| Oral herpes                                           |                  |  |  |

|                             |                |  |  |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 2 / 26 (7.69%) |  |  |
| occurrences (all)           | 2              |  |  |
| Syphilis                    |                |  |  |
| subjects affected / exposed | 2 / 26 (7.69%) |  |  |
| occurrences (all)           | 2              |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment                                                                                                                                                                                                                                                                                                                                                                                            |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 21 January 2015 | <ul style="list-style-type: none"><li>• Additional exclusion period for the use of investigational drugs or devices to meet German regulatory preferences.</li><li>• Clarification of contraceptive requirements.</li></ul>                                                                                                                                                                          |
| 05 March 2015   | Clarification that subjects may not have antiretroviral regimens changed to support entry to the trial.                                                                                                                                                                                                                                                                                              |
| 30 March 2015   | Added aniodarone to the "Agents Disallowed" list based on risk of symptomatic bradycardia with coadministration of amiodarone with ledipasvir/sofosbuvir. Postmarketing cases of symptomatic bradycardia have been reported in patients receiving amiodarone who were coadministered Harvoni® (ledipasvir/sofosbuvir), or Sovaldi® (sofosbuvir) in combination with another direct acting antiviral. |

Notes:

---

### 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: