



## Clinical trial results:

### A Phase 1 Relative Bioavailability and Food Effect Study of a Pediatric Granules Formulation of Ledipasvir/Sofosbuvir in Healthy Adult Subjects

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2015-003570-32 |
| Trial protocol           | Outside EU/EEA |
| Global end of trial date | 30 June 2015   |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 15 July 2016 |
| First version publication date | 15 July 2016 |

#### Trial information

##### Trial identification

|                       |                |
|-----------------------|----------------|
| Sponsor protocol code | GS-US-337-1115 |
|-----------------------|----------------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Gilead Sciences   |
| Sponsor organisation address | 333 Lakeside Drive, Foster City, United States,   |
| Public contact               | Clinical Trial Mailbox, Gilead Sciences International Ltd,<br>ClinicalTrialDisclosures@gilead.com |
| Scientific contact           | Clinical Trial Mailbox, Gilead Sciences International Ltd,<br>ClinicalTrialDisclosures@gilead.com |

Notes:

#### Paediatric regulatory details

|  |                     |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP)       | Yes                 |
| EMA paediatric investigation plan number(s)                          | EMA-001411-PIP01-12 |
| 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                       | 30 June 2015 |
| Is this the analysis of the primary completion data? | No           |
| Global end of trial reached?                         | Yes          |
| Global end of trial date                             | 30 June 2015 |
| Was the trial ended prematurely?                     | No           |

Notes:

## General information about the trial

Main objective of the trial:

This study was to evaluate the relative bioavailability of a pediatric granules formulation of ledipasvir/sofosbuvir (LDV/SOF) relative to tablet formulation in healthy participants and to evaluate the effect of concomitant food intake on the pharmacokinetics of a pediatric granules formulation of LDV/SOF.

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                          | 13 May 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 States: 42 |
| Worldwide total number of subjects   | 42                |
| EEA total number of subjects         | 0                 |

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)      | 42 |
| From 65 to 84 years       | 0  |
| 85 years and over         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Participants were enrolled at study sites in the United States. The first participant was screened on 13 May 2015. The last study visit occurred on 30 June 2015.

### Pre-assignment

Screening details:

63 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

|           |                      |
|-----------|----------------------|
| Arm title | Overall Participants |
|-----------|----------------------|

Arm description:

Participants were randomized to 1 of 6 treatment sequences and received each of the following treatments with a 9-day washout interval between each treatment:

- Treatment A: Single dose of LDV/SOF tablet administered under fasted conditions
- Treatment B: Single dose of LDV/SOF oral granules administered under fasted conditions
- Treatment C: Single dose of LDV/SOF oral granules administered under fed conditions

|  |                       |
|--|-----------------------|
| Arm type                               | Experimental          |
| Investigational medicinal product name | Ledipasvir/sofosbuvir |
| Investigational medicinal product code | Harvoni®; LDV/SOF     |
| Other name                             |                       |
| Pharmaceutical forms                   | Granules, Tablet      |
| Routes of administration               | Oral use              |

Dosage and administration details:

1 x 90/400 mg tablet or 90/400 mg (8 x 11.25/50 mg units) granules administered orally under fasted or fed conditions

|                                       |                      |
|---------------------------------------|----------------------|
| <b>Number of subjects in period 1</b> | Overall Participants |
| Started                               | 42                   |
| Completed                             | 42                   |

## Baseline characteristics

### Reporting groups

|                       |                      |
|-----------------------|----------------------|
| Reporting group title | Overall Participants |
|-----------------------|----------------------|

Reporting group description:

Participants were randomized to 1 of 6 treatment sequences and received each of the following treatments with a 9-day washout interval between each treatment:

- Treatment A: Single dose of LDV/SOF tablet administered under fasted conditions
- Treatment B: Single dose of LDV/SOF oral granules administered under fasted conditions
- Treatment C: Single dose of LDV/SOF oral granules administered under fed conditions

| Reporting group values                | Overall Participants | Total |  |
|---------------------------------------|----------------------|-------|--|
| Number of subjects                    | 42                   | 42    |  |
| Age categorical<br>Units: Subjects    |                      |       |  |
| Adults (18-64 years)                  | 42                   | 42    |  |
| Gender categorical<br>Units: Subjects |                      |       |  |
| Female                                | 21                   | 21    |  |
| Male                                  | 21                   | 21    |  |
| Race<br>Units: Subjects               |                      |       |  |
| Asian                                 | 1                    | 1     |  |
| Black or African American             | 2                    | 2     |  |
| White                                 | 39                   | 39    |  |
| Ethnicity<br>Units: Subjects          |                      |       |  |
| Hispanic or Latino                    | 41                   | 41    |  |
| Not Hispanic or Latino                | 1                    | 1     |  |

## End points

### End points reporting groups

|                       |                      |
|-----------------------|----------------------|
| Reporting group title | Overall Participants |
|-----------------------|----------------------|

Reporting group description:

Participants were randomized to 1 of 6 treatment sequences and received each of the following treatments with a 9-day washout interval between each treatment:

- Treatment A: Single dose of LDV/SOF tablet administered under fasted conditions
- Treatment B: Single dose of LDV/SOF oral granules administered under fasted conditions
- Treatment C: Single dose of LDV/SOF oral granules administered under fed conditions

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | Treatment A        |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Ledipasvir/sofosbuvir 90/400 mg (1 x 90/400 mg tablet) administered orally under fasted conditions

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | Treatment B        |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Ledipasvir/sofosbuvir 90/400 mg (8 x 11.25/50 mg units, LDV/SOF oral granules) administered orally under fasted conditions

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | Treatment C        |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Ledipasvir/sofosbuvir 90/400 mg (8 x 11.25/50 mg units, LDV/SOF oral granules) administered orally under fed conditions

### Primary: PK Parameter of LDV as measured by Cmax

|                 |   |
|-----------------|---|
| End point title | PK Parameter of LDV as measured by Cmax |
|-----------------|---|

End point description:

Cmax was defined as maximum observed plasma concentration of drug. PK Analysis Set: participants who received at least 1 dose of study drug and had at least 1 non-missing PK concentration data reported by PK lab for each respective analyte.

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

End point timeframe:

Predose ( $\leq 5$  minutes), 0.25, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 6, 8, 10, 12, 16, 20, 24, 48, 72, 96, 120, and 144 hours postdose on Days 1, 11, and 21

| End point values                         | Treatment A             | Treatment B            | Treatment C          |  |
|--|-------------------------|------------------------|----------------------|--|
| Subject group type                       | Subject analysis set    | Subject analysis set   | Subject analysis set |  |
| Number of subjects analysed              | 42                      | 40                     | 42                   |  |
| Units: Participants                      |                         |                        |                      |  |
| geometric mean (confidence interval 95%) | 274.41 (234.5 to 321.1) | 163.9 (145.5 to 184.5) | 216 (200.8 to 232.3) |  |

## Statistical analyses

|   |                                       |
|---|---------------------------------------|
| <b>Statistical analysis title</b>   | LDV: Treatment B/Treatment A for Cmax |
| Statistical analysis description:<br>A parametric mixed effect analysis of variance (ANOVA) model was used to estimate the geometric least-squares mean (GLSM) ratio (Treatment B/Treatment A) of the PK parameter and the corresponding 90% CI. Bioequivalence was concluded if the 90% CIs fell within the prespecified boundaries of 80% to 125%. "Subjects in this analysis" states 82; however, participants analyzed in PK analysis set were 40 for Treatment B and 42 for Treatment A. |                                       |
| Comparison groups   | Treatment A v Treatment B             |
| Number of subjects included in analysis   | 82                                    |
| Analysis specification  | Pre-specified                         |
| Analysis type   | other                                 |
| Parameter estimate  | Geometric least-squares mean ratio    |
| Point estimate  | 59.53                                 |
| Confidence interval   |                                       |
| level   | 90 %                                  |
| sides   | 2-sided                               |
| lower limit   | 52.71                                 |
| upper limit   | 67.24                                 |

## Primary: PK Parameter of GS-331007 (SOF metabolite) as measured by Cmax

|   |  |
|---|--|
| End point title   | PK Parameter of GS-331007 (SOF metabolite) as measured by Cmax |
| End point description:  |  |
| End point type  | Primary  |
| End point timeframe:<br>Predose ( $\leq 5$ minutes), 0.25, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 6, 8, 10, 12,16, 20, 24, 48, 72, 96, 120, and 144 hours postdose on Days 1, 11, and 21 |  |

| End point values                         | Treatment A            | Treatment B             | Treatment C            |  |
|--|------------------------|-------------------------|------------------------|--|
| Subject group type                       | Subject analysis set   | Subject analysis set    | Subject analysis set   |  |
| Number of subjects analysed              | 42                     | 40                      | 42                     |  |
| Units: Participants                      |                        |                         |                        |  |
| geometric mean (confidence interval 95%) | 826.8 (771.6 to 886.1) | 959.8 (890.6 to 1034.5) | 537.6 (507.6 to 569.4) |  |

## Statistical analyses

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | GS-331007: Treatment B/Treatment A for Cmax |
| Statistical analysis description:<br>A parametric mixed effect ANOVA model was used to estimate the GLSM ratio (Treatment B/Treatment A) of the PK parameter and the corresponding 90% CI. Bioequivalence was concluded if the 90% CIs fell within the prespecified boundaries of 80% to 125%. "Subjects in this analysis" states 82; however participants in analyzed in PK analysis were 40 for Treatment B and 42 for Treatment A. |   |

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | Treatment A v Treatment B          |
| Number of subjects included in analysis | 82                                 |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           | other                              |
| Parameter estimate                      | Geometric least-squares mean ratio |
| Point estimate                          | 115.31                             |
| Confidence interval                     |                                    |
| level                                   | 90 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | 109.31                             |
| upper limit                             | 121.64                             |

### Primary: PK Parameter of LDV as measured by AUClast and AUCinf

|                 |   |
|-----------------|---|
| End point title | PK Parameter of LDV as measured by AUClast and AUCinf |
|-----------------|---|

End point description:

- AUClast was defined as area under the plasma concentration-time curve from time 0 to the last measurable concentration.
- AUCinf was defined as area under the plasma concentration-time curve from time zero to infinity.

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

End point timeframe:

Predose ( $\leq 5$  minutes), 0.25, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 6, 8, 10, 12, 16, 20, 24, 48, 72, 96, 120, and 144 hours postdose on Days 1, 11, and 21

| End point values                         | Treatment A               | Treatment B               | Treatment C                |  |
|--|---------------------------|---------------------------|----------------------------|--|
| Subject group type                       | Subject analysis set      | Subject analysis set      | Subject analysis set       |  |
| Number of subjects analysed              | 42                        | 40                        | 42                         |  |
| Units: Participants                      |                           |                           |                            |  |
| geometric mean (confidence interval 95%) |                           |                           |                            |  |
| AUClast                                  | 7939.8 (6762.3 to 9322.3) | 4863.9 (4299.4 to 5502.5) | 6451.6 (5956.7 to 69857.5) |  |
| AUCinf                                   | 9257 (7824.5 to 10951.9)  | 5763.9 (5044.3 to 6586.1) | 7553.4 (6860.5 to 8316.4)  |  |

### Statistical analyses

|                            |  |
|----------------------------|--|
| Statistical analysis title | LDV: Treatment B/Treatment A for AUClast |
|----------------------------|--|

Statistical analysis description:

A parametric mixed effect ANOVA model was used to estimate the GLSM ratio (Treatment B/Treatment A) of the PK parameter and the corresponding 90% CI. Bioequivalence was concluded if the 90% CIs fell within the prespecified boundaries of 80% to 125%. "Subjects in this analysis" states 82; however, participants analyzed in PK analysis set were 40 for Treatment B and 42 for Treatment A.

|                   |                           |
|-------------------|---------------------------|
| Comparison groups | Treatment B v Treatment A |
|-------------------|---------------------------|



|   |                                    |
|---|------------------------------------|
| Number of subjects included in analysis | 82                                 |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           | other                              |
| Parameter estimate                      | Geometric least-squares mean ratio |
| Point estimate                          | 60.96                              |
| Confidence interval                     |                                    |
| level                                   | 90 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | 54.72                              |
| upper limit                             | 67.91                              |

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | LDV: Treatment C/Treatment B for AUClast |
|-----------------------------------|--|

Statistical analysis description:

A parametric mixed effect ANOVA model was used to estimate the GLSM ratio (Treatment C/Treatment B) of the PK parameter and the corresponding 90% CI. PK equivalence was concluded if the 90% CIs fell within the prespecified boundaries of 70% to 143%. "Subjects in this analysis" states 82; however, participants analyzed in PK analysis set were 42 for Treatment C and 40 for Treatment B.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | Treatment B v Treatment C          |
| Number of subjects included in analysis | 82                                 |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           | other                              |
| Parameter estimate                      | Geometric least-squares mean ratio |
| Point estimate                          | 134.79                             |
| Confidence interval                     |                                    |
| level                                   | 90 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | 123.55                             |
| upper limit                             | 147.05                             |

|                                   |   |
|-----------------------------------|---|
| <b>Statistical analysis title</b> | LDV: Treatment B/Treatment A for AUCinf |
|-----------------------------------|---|

Statistical analysis description:

A parametric mixed effect ANOVA model was used to estimate the GLSM ratio (Treatment B/Treatment A) of the PK parameter and the corresponding 90% CI. Bioequivalence was concluded if the 90%

CIs fell within the prespecified boundaries of 80% to 125%. "Subjects in this analysis" states 82; however, participants analyzed in PK analysis set were 40 for Treatment B and 42 for Treatment A.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | Treatment B v Treatment A          |
| Number of subjects included in analysis | 82                                 |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           | other                              |
| Parameter estimate                      | Geometric least-squares mean ratio |
| Point estimate                          | 61.86                              |
| Confidence interval                     |                                    |
| level                                   | 90 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | 55.38                              |
| upper limit                             | 69.1                               |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | LDV: Treatment C/Treatment B for AUCinf |
| Statistical analysis description:<br>A parametric mixed effect ANOVA model was used to estimate the GLSM ratio (Treatment C/Treatment B) of the PK parameter and the corresponding 90% CI. PK equivalence was concluded if the 90% CIs fell within the prespecified boundaries of 70% to 143%. "Subjects in this analysis" states 82; however, participants analyzed in PK analysis set were 40 for Treatment C and 42 for Treatment B. |   |
| Comparison groups   | Treatment B v Treatment C               |
| Number of subjects included in analysis   | 82                                      |
| Analysis specification  | Pre-specified                           |
| Analysis type   | other                                   |
| Parameter estimate  | Geometric least-squares mean ratio      |
| Point estimate  | 133.51                                  |
| Confidence interval   |   |
| level   | 90 %                                    |
| sides   | 2-sided                                 |
| lower limit   | 122.31                                  |
| upper limit   | 145.75                                  |

**Primary: PK Parameter of GS-331007 (SOF metabolite) as measured by AUClast and AUCinf**

|   |  |
|---|--|
| End point title   | PK Parameter of GS-331007 (SOF metabolite) as measured by AUClast and AUCinf |
| End point description:  |  |
| End point type  | Primary  |
| End point timeframe:<br>Predose ( $\leq 5$ minutes), 0.25, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 6, 8, 10, 12,16, 20, 24, 48, 72, 96, 120, and 144 hours postdose on Days 1, 11, and 21 |  |

| <b>End point values</b>                  | Treatment A                     | Treatment B                   | Treatment C                     |  |
|--|---------------------------------|-------------------------------|---------------------------------|--|
| Subject group type                       | Subject analysis set            | Subject analysis set          | Subject analysis set            |  |
| Number of subjects analysed              | 42                              | 40                            | 42                              |  |
| Units: Participants                      |                                 |                               |                                 |  |
| geometric mean (confidence interval 95%) |                                 |                               |                                 |  |
| AUClast                                  | 10418.5<br>(9727.2 to 11158.9)  | 10897.8<br>(10121.2 to 11734) | 11999.5<br>(11330.9 to 12707.5) |  |
| AUCinf                                   | 10958.4<br>(10257.8 to 11706.8) | 11438.5<br>(10640 to 12296.9) | 12640.5<br>(11972.5 to 13345.7) |  |

## Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>   | GS-331007: Treatment B/Treatment A for AUClast |
| Statistical analysis description:<br>A parametric mixed effect ANOVA model was used to estimate the GLSM ratio (Treatment B/Treatment A) of the PK parameter and the corresponding 90% CI. Bioequivalence was concluded if the 90% CIs fell within the prespecified boundaries of 80% to 125%. "Subjects in this analysis" states 82; however, participants analyzed in PK analysis set were 40 for Treatment B and 42 for Treatment A. |  |
| Comparison groups   | Treatment A v Treatment B                      |
| Number of subjects included in analysis   | 82   |
| Analysis specification  | Pre-specified                                  |
| Analysis type   | other  |
| Parameter estimate  | Geometric least-squares mean ratio             |
| Point estimate  | 103.38   |
| Confidence interval   |  |
| level   | 90 %   |
| sides   | 2-sided  |
| lower limit   | 99.63  |
| upper limit   | 107.27   |

|   |  |
|---|--|
| <b>Statistical analysis title</b>   | GS-331007: Treatment C/Treatment B for AUClast |
| Statistical analysis description:<br>A parametric mixed effect ANOVA model was used to estimate the GLSM ratio (Treatment C/Treatment B) of the PK parameter and the corresponding 90% CI. PK equivalence was concluded if the 90% CIs fell within the prespecified boundaries of 80% to 125%. "Subjects in this analysis" states 82; however, participants analyzed in PK analysis set were 42 for Treatment C and 40 for Treatment B. |  |
| Comparison groups   | Treatment B v Treatment C                      |
| Number of subjects included in analysis   | 82   |
| Analysis specification  | Pre-specified                                  |
| Analysis type   | other  |
| Parameter estimate  | Geometric least-squares mean ratio             |
| Point estimate  | 111.03   |
| Confidence interval   |  |
| level   | 90 %   |
| sides   | 2-sided  |
| lower limit   | 106.44   |
| upper limit   | 115.83   |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | GS-331007: Treatment B/Treatment A for AUCinf |
| Statistical analysis description:<br>A parametric mixed effect ANOVA model was used to estimate the GLSM ratio (Treatment B/Treatment A) of the PK parameter and the corresponding 90% CI. Bioequivalence was concluded if the 90% CIs fell within the prespecified boundaries of 80% to 125%. "Subjects in this analysis" states 82; however, participants analyzed in PK analysis set were 40 for Treatment B and 42 for Treatment A. |   |
| Comparison groups   | Treatment B v Treatment A                     |

|   |                                    |
|---|------------------------------------|
| Number of subjects included in analysis | 82                                 |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           | other                              |
| Parameter estimate                      | Geometric least-squares mean ratio |
| Point estimate                          | 103.13                             |
| Confidence interval                     |                                    |
| level                                   | 90 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | 99.5                               |
| upper limit                             | 106.9                              |

|                                   |   |
|-----------------------------------|---|
| <b>Statistical analysis title</b> | GS-331007: Treatment C/Treatment B for AUCinf |
|-----------------------------------|---|

Statistical analysis description:

A parametric mixed effect ANOVA model was used to estimate the GLSM ratio (Treatment C/Treatment B) of the PK parameter and the corresponding 90% CI. PK equivalence was concluded if the 90% CIs fell within the prespecified boundaries of 80% to 125%. "Subjects in this analysis" states 82; however, participants analyzed in PK analysis set were 42 for Treatment C and 40 for Treatment B.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | Treatment B v Treatment C          |
| Number of subjects included in analysis | 82                                 |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           | other                              |
| Parameter estimate                      | Geometric least-squares mean ratio |
| Point estimate                          | 111.45                             |
| Confidence interval                     |                                    |
| level                                   | 90 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | 106.89                             |
| upper limit                             | 116.21                             |

## Adverse events

### Adverse events information<sup>[1]</sup>

Timeframe for reporting adverse events:

Up to 21 days plus 30 days

Adverse event reporting additional description:

Safety Analysis Set included all randomized subjects who received at least 1 dose of study drug.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 18.0 |
|--------------------|------|

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Treatment A |
|-----------------------|-------------|

Reporting group description:

Ledipasvir/sofosbuvir 90/400 mg (1 x 90/400 mg tablet) administered orally under fasted conditions

|                       |             |
|-----------------------|-------------|
| Reporting group title | Treatment B |
|-----------------------|-------------|

Reporting group description:

Ledipasvir/sofosbuvir 90/400 mg (8 x 11.25/50 mg units, LDV/SOF oral granules) administered orally under fasted conditions

|                       |             |
|-----------------------|-------------|
| Reporting group title | Treatment C |
|-----------------------|-------------|

Reporting group description:

Ledipasvir/sofosbuvir 90/400 mg (8 x 11.25/50 mg units, LDV/SOF oral granules) administered orally under fed conditions

| Serious adverse events                            | Treatment A    | Treatment B    | Treatment C    |
|---|----------------|----------------|----------------|
| Total subjects affected by serious adverse events |                |                |                |
| subjects affected / exposed                       | 0 / 42 (0.00%) | 0 / 42 (0.00%) | 0 / 42 (0.00%) |
| number of deaths (all causes)                     | 0              | 0              | 0              |
| number of deaths resulting from adverse events    | 0              | 0              | 0              |

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

| Non-serious adverse events                            | Treatment A    | Treatment B    | Treatment C    |
|---|----------------|----------------|----------------|
| Total subjects affected by non-serious adverse events |                |                |                |
| subjects affected / exposed                           | 0 / 42 (0.00%) | 0 / 42 (0.00%) | 0 / 42 (0.00%) |

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: None of the non-serious AE preferred terms occurred to at least 5% of subjects in any of the treatment groups.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

---

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

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

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

Notes: