



Clinical trial results:

A Phase 2, Multicenter, Open-Label Study to Evaluate the Efficacy and Safety of Sofosbuvir/Velpatasvir Fixed Dose Combination in Subjects with Chronic HCV Infection who have Received a Liver Transplant

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2016-000416-15 |
| Trial protocol | GB |
| Global end of trial date | 28 July 2017 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 (current) |
| This version publication date | 10 August 2018 |
| First version publication date | 10 August 2018 |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | GS-US-342-2104 |
|-----------------------|----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02781571 |
| 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 | 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 | 28 July 2017 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 28 July 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 28 July 2017 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study were to evaluate the efficacy, safety, and tolerability of sofosbuvir /velpatasvir (SOF/VEL) fixed-dose combination (FDC) in participants with chronic hepatitis C virus (HCV) who have received a liver transplant.

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 | 27 July 2016 |
| 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 | Spain: 31 |
| Country: Number of subjects enrolled | United Kingdom: 41 |
| Country: Number of subjects enrolled | Switzerland: 7 |
| Worldwide total number of subjects | 79 |
| EEA total number of subjects | 72 |

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) | 47 |
| From 65 to 84 years | 32 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Spain, Switzerland, and the United Kingdom. The first participant was screened on 27 July 2016. The last study visit occurred on 28 July 2017.

Pre-assignment

Screening details:

85 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

| | |
|-----------|---------|
| Arm title | SOF/VEL |
|-----------|---------|

Arm description:

SOF/VEL in participants with chronic HCV infection who received a liver transplant

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

Dosage and administration details:

400/100 mg FDC once daily for 12 weeks

| Number of subjects in period 1 | SOF/VEL |
|--------------------------------|---------|
| Started | 79 |
| Completed | 79 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------------|
| Reporting group title | Overall Study |
|-----------------------|---------------|

Reporting group description:

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

| Reporting group values | Overall Study | Total | |
|---|---------------|-------|--|
| Number of subjects | 79 | 79 | |
| Age categorical Units: Subjects | | | |
| Age continuous Units: years arithmetic mean standard deviation | 62 ± 8.7 | - | |
| Gender categorical Units: Subjects | | | |
| Female | 15 | 15 | |
| Male | 64 | 64 | |
| Race Units: Subjects | | | |
| Black or African American | 2 | 2 | |
| White | 65 | 65 | |
| Asian | 12 | 12 | |
| Ethnicity Units: Subjects | | | |
| Hispanic or Latino | 2 | 2 | |
| Not Hispanic or Latino | 77 | 77 | |
| IL28b Status | | | |
| The CC, CT, and TT alleles are different forms of the IL28b gene. | | | |
| Units: Subjects | | | |
| CC | 39 | 39 | |
| CT | 34 | 34 | |
| TT | 6 | 6 | |
| HCV Genotype Units: Subjects | | | |
| Genotype 1 | 37 | 37 | |
| Genotype 2 | 3 | 3 | |
| Genotype 3 | 35 | 35 | |
| Genotype 4 | 4 | 4 | |
| HCV RNA Category Units: Subjects | | | |
| < 800,000 IU/mL | 18 | 18 | |
| ≥ 800,000 IU/mL | 61 | 61 | |

| | | | |
|--------------------|--------|---|--|
| HCV RNA | | | |
| Units: log10 IU/mL | | | |
| arithmetic mean | 6.4 | | |
| standard deviation | ± 0.55 | - | |

End points

End points reporting groups

| | |
|--|---------|
| Reporting group title | SOF/VEL |
| Reporting group description: SOF/VEL in participants with chronic HCV infection who received a liver transplant | |

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

| | |
|---|---|
| End point title | Percentage of Participants With Sustained Virologic Response (SVR) 12 Weeks After Cessation of Therapy (SVR12) ^[1] |
| 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 enrolled participants who took at least 1 dose of the 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: No statistical comparison was planned or performed. | |

| End point values | SOF/VEL | | | |
|-----------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 79 | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 96.2 (89.3 to 99.2) | | | |

Statistical analyses

No statistical analyses for this end point

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

| | |
|---|--|
| End point title | Percentage of Participants Who Permanently Discontinued Study Drug Due to Any Adverse Event ^[2] |
| End point description: Safety Analysis Set: participants who took at least 1 dose of the study drug. | |
| End point type | Primary |
| End point timeframe: Up to 12 weeks | |

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical comparison was planned or performed.

| End point values | SOF/VEL | | | |
|-----------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 79 | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 1.3 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Sustained Virologic Response 4 Weeks After Cessation of Therapy (SVR4)

| | |
|-----------------|--|
| End point title | Percentage of Participants With Sustained Virologic Response 4 Weeks After Cessation of Therapy (SVR4) |
|-----------------|--|

End point description:

SVR4 was defined as HCV RNA < LLOQ at 4 weeks after stopping study treatment. Participants in the Full Analysis Set were analyzed.

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

End point timeframe:

Posttreatment Week 4

| End point values | SOF/VEL | | | |
|-----------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 79 | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 97.5 (91.2 to 99.7) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HCV RNA < LLOQ at Week 2

| | |
|-----------------|--|
| End point title | Percentage of Participants With HCV RNA < LLOQ at Week 2 |
|-----------------|--|

End point description:

Participants in the Full Analysis Set were analyzed.

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

End point timeframe:

Week 2

| | | | | |
|-----------------------------------|---------------------|--|--|--|
| End point values | SOF/VEL | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 79 | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 40.5 (29.6 to 52.1) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HCV RNA < LLOQ at Week 4

| | |
|------------------------|--|
| End point title | Percentage of Participants With HCV RNA < LLOQ at Week 4 |
| End point description: | Participants in the Full Analysis Set with available data were analyzed. |
| End point type | Secondary |
| End point timeframe: | Week 4 |

| | | | | |
|-----------------------------------|---------------------|--|--|--|
| End point values | SOF/VEL | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 78 | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 85.9 (76.2 to 92.7) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HCV RNA < LLOQ at Week 8

| | |
|------------------------|--|
| End point title | Percentage of Participants With HCV RNA < LLOQ at Week 8 |
| End point description: | Participants in the Full Analysis Set with available data were analyzed. |
| End point type | Secondary |
| End point timeframe: | Week 8 |

| | | | | |
|-----------------------------------|----------------------|--|--|--|
| End point values | SOF/VEL | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 78 | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 98.7 (93.1 to 100.0) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HCV RNA < LLOQ at Week 12

| | |
|------------------------|--|
| End point title | Percentage of Participants With HCV RNA < LLOQ at Week 12 |
| End point description: | Participants in the Full Analysis Set with available data were analyzed. |
| End point type | Secondary |
| End point timeframe: | Week 12 |

| | | | | |
|-----------------------------------|-----------------------|--|--|--|
| End point values | SOF/VEL | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 78 | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 100.0 (95.4 to 100.0) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: HCV RNA at Week 2

| | |
|------------------------|--|
| End point title | HCV RNA at Week 2 |
| End point description: | Participants in the Full Analysis Set with available data were analyzed. |
| End point type | Secondary |
| End point timeframe: | Week 2 |

| | | | | |
|--------------------------------------|---------------------|--|--|--|
| End point values | SOF/VEL | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 75 | | | |
| Units: log10 IU/mL | | | | |
| arithmetic mean (standard deviation) | 1.59 (\pm 0.596) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: HCV RNA at Week 4

| | |
|------------------------|--|
| End point title | HCV RNA at Week 4 |
| End point description: | Participants in the Full Analysis Set with available data were analyzed. |
| End point type | Secondary |
| End point timeframe: | Week 4 |

| | | | | |
|--------------------------------------|---------------------|--|--|--|
| End point values | SOF/VEL | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 78 | | | |
| Units: log10 IU/mL | | | | |
| arithmetic mean (standard deviation) | 1.23 (\pm 0.251) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: HCV RNA at Week 8

| | |
|------------------------|--|
| End point title | HCV RNA at Week 8 |
| End point description: | Participants in the Full Analysis Set with available data were analyzed. |
| End point type | Secondary |
| End point timeframe: | Week 8 |

| End point values | SOF/VEL | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 77 | | | |
| Units: log10 IU/mL | | | | |
| arithmetic mean (standard deviation) | 1.15 (± 0.00) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: HCV RNA at Week 12

| | |
|------------------------|--|
| End point title | HCV RNA at Week 12 |
| End point description: | Participants in the Full Analysis Set with available data were analyzed. |
| End point type | Secondary |
| End point timeframe: | Week 12 |

| End point values | SOF/VEL | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 78 | | | |
| Units: log10 IU/mL | | | | |
| arithmetic mean (standard deviation) | 1.15 (± 0.00) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in HCV RNA at Week 2

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

| End point values | SOF/VEL | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 75 | | | |
| Units: log10 IU/mL | | | | |
| arithmetic mean (standard deviation) | -4.75 (± 0.635) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in HCV RNA at Week 4

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

| End point values | SOF/VEL | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 78 | | | |
| Units: log10 IU/mL | | | | |
| arithmetic mean (standard deviation) | -5.13 (± 0.551) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in HCV RNA at Week 8

| | |
|--|---|
| End point title | Change From Baseline in HCV RNA at Week 8 |
| End point description: Participants in the Full Analysis Set with available data were analyzed. | |
| End point type | Secondary |
| End point timeframe: Baseline; Week 8 | |

| End point values | SOF/VEL | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 77 | | | |
| Units: log10 IU/mL | | | | |
| arithmetic mean (standard deviation) | -5.20 (± 0.548) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in HCV RNA at Week 12

| | |
|--|--|
| End point title | Change From Baseline in HCV RNA at Week 12 |
| End point description: Participants in the Full Analysis Set with available data were analyzed. | |
| End point type | Secondary |
| End point timeframe: Baseline; Week 12 | |

| End point values | SOF/VEL | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 78 | | | |
| Units: log10 IU/mL | | | | |
| arithmetic mean (standard deviation) | -5.22 (± 0.554) | | | |

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: Breakthrough (confirmed HCV RNA ≥ LLOQ after having previously had HCV RNA < LLOQ on 2 consecutive measurements while on treatment), or Rebound (confirmed > 1 log10 IU/mL increase in HCV RNA from nadir while on treatment), or Non-response (HCV RNA persistently ≥ LLOQ through 12 weeks of treatment) • Virologic relapse: HCV RNA ≥ LLOQ during the post-treatment period having achieved HCV RNA < LLOQ at end of treatment, confirmed with 2 consecutive values or last available post-treatment measurement. Participants in the Full Analysis Set were analyzed. | |
| End point type | Secondary |

End point timeframe:

Up to Posttreatment Week 12

| | | | | |
|-----------------------------------|-----------------|--|--|--|
| End point values | SOF/VEL | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 79 | | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 2.5 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 12 weeks plus 30 days

Adverse event reporting additional description:

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

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

Dictionary used

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

| | |
|--------------------|----|
| Dictionary version | 20 |
|--------------------|----|

Reporting groups

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

Reporting group description:

SOF/VEL in participants with chronic HCV infection who received a liver transplant

| Serious adverse events | SOF/VEL | | |
|---|----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 79 (3.80%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Hepatocellular carcinoma | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Joint swelling | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Pneumonia klebsiella | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| 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 %

| Non-serious adverse events | SOF/VEL | | |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 42 / 79 (53.16%) | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 19 / 79 (24.05%) | | |
| occurrences (all) | 19 | | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 16 / 79 (20.25%) | | |
| occurrences (all) | 16 | | |
| Asthenia | | | |
| subjects affected / exposed | 5 / 79 (6.33%) | | |
| occurrences (all) | 5 | | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 6 / 79 (7.59%) | | |
| occurrences (all) | 6 | | |
| Nausea | | | |
| subjects affected / exposed | 6 / 79 (7.59%) | | |
| occurrences (all) | 6 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 8 / 79 (10.13%) | | |
| occurrences (all) | 8 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Myalgia | | | |
| subjects affected / exposed | 4 / 79 (5.06%) | | |
| occurrences (all) | 5 | | |
| Infections and infestations | | | |
| Influenza | | | |
| subjects affected / exposed | 5 / 79 (6.33%) | | |
| occurrences (all) | 6 | | |
| Viral upper respiratory tract infection | | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 5 / 79 (6.33%) 5 | | |
| Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) | 4 / 79 (5.06%) 4 | | |

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

None reported