



Clinical trial results:

A Phase 3, Multicenter, Randomized, Open-Label Study to Compare the Efficacy and Safety of Sofosbuvir/GS-5816 Fixed Dose Combination for 12 Weeks with Sofosbuvir and Ribavirin for 24 Weeks in Subjects with Chronic Genotype 3 HCV Infection

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2014-001682-27 |
| Trial protocol | GB IT FR |
| Global end of trial date | 15 December 2015 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 11 November 2016 |
| First version publication date | 11 November 2016 |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | GS-US-342-1140 |
|-----------------------|----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02201953 |
| 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 Trial Mailbox, Gilead Sciences International Ltd, ClinicalTrialDisclosures@gilead.com |
| Scientific contact | Clinical Trial Mailbox, Gilead Sciences International Ltd, 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 | 15 December 2015 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 15 December 2015 |
| 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 compare the efficacy of treatment with sofosbuvir/velpatasvir (SOF/VEL) fixed-dose combination (FDC) for 12 weeks with that of sofosbuvir (SOF) + ribavirin (RBV) for 24 weeks and to evaluate the safety and tolerability of each treatment regimen in participants with chronic genotype 3 hepatitis C virus (HCV) infection.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 25 June 2014 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|---------------------|
| Country: Number of subjects enrolled | United Kingdom: 108 |
| Country: Number of subjects enrolled | France: 102 |
| Country: Number of subjects enrolled | Germany: 66 |
| Country: Number of subjects enrolled | Italy: 18 |
| Country: Number of subjects enrolled | New Zealand: 17 |
| Country: Number of subjects enrolled | Canada: 33 |
| Country: Number of subjects enrolled | United States: 121 |
| Country: Number of subjects enrolled | Australia: 93 |
| Worldwide total number of subjects | 558 |
| EEA total number of subjects | 294 |

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) | 537 |
| From 65 to 84 years | 21 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Australia, North America, Europe, and New Zealand. The first participant was screened on 14 July 2014. The last study visit occurred on 15 December 2015.

Pre-assignment

Screening details:

652 participants were screened.

Period 1

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

Arms

| | |
|------------------------------|------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | SOF/VEL 12 Weeks |

Arm description:

SOF/VEL for 12 weeks

| | |
|--|---------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Sofosbuvir/velpatasvir |
| Investigational medicinal product code | |
| Other name | Epclusa®, GS-7977/GS-5816 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

400/100 mg FDC tablet administered once daily

| | |
|------------------|------------------|
| Arm title | SOF+RBV 24 Weeks |
|------------------|------------------|

Arm description:

SOF+RBV for 24 weeks

| | |
|--|-----------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Sofosbuvir |
| Investigational medicinal product code | |
| Other name | Sovaldi®, GS-7977, PSI-7977 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

400 mg administered once daily

| | |
|--|-----------|
| Investigational medicinal product name | Ribavirin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Administered in a divided daily dose according to package insert weight-based dosing recommendations (< 75 kg = 1000 mg and ≥ 75 kg = 1200 mg)

| Number of subjects in period 1^[1] | SOF/VEL 12 Weeks | SOF+RBV 24 Weeks |
|---|-------------------------|-------------------------|
| Started | 277 | 275 |
| Completed | 258 | 224 |
| Not completed | 19 | 51 |
| Adverse event, serious fatal | - | 2 |
| Withdrew Consent | 2 | 5 |
| Adverse event, non-fatal | - | 5 |
| Death | - | 1 |
| Lost to follow-up | 8 | 8 |
| Lack of efficacy | 9 | 30 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 6 participants (SOF/VEL 12 Weeks = 1; SOF+RBV 24 Weeks = 5) who were randomized but not treated are not included in the subject disposition table.

Baseline characteristics

Reporting groups

| | |
|--|------------------|
| Reporting group title | SOF/VEL 12 Weeks |
| Reporting group description: SOF/VEL for 12 weeks | |
| Reporting group title | SOF+RBV 24 Weeks |
| Reporting group description: SOF+RBV for 24 weeks | |

| Reporting group values | SOF/VEL 12 Weeks | SOF+RBV 24 Weeks | Total |
|------------------------------------|------------------|------------------|-------|
| Number of subjects | 277 | 275 | 552 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|--------------|------------|-----|
| Age continuous Units: years arithmetic mean standard deviation | 49 ± 10.4 | 50 ± 10 | - |
| Gender categorical Units: Subjects | | | |
| Female | 107 | 101 | 208 |
| Male | 170 | 174 | 344 |
| Ethnicity Units: Subjects | | | |
| Hispanic or Latino | 11 | 11 | 22 |
| Not Hispanic or Latino | 266 | 263 | 529 |
| Not Disclosed | 0 | 1 | 1 |
| Race Units: Subjects | | | |
| Black or African American | 3 | 1 | 4 |
| White | 250 | 239 | 489 |
| Asian | 23 | 29 | 52 |
| American Indian or Alaska Native | 1 | 3 | 4 |
| Native Hawaiian or Pacific Islander | 0 | 2 | 2 |
| Not Disclosed | 0 | 1 | 1 |
| HCV Genotype Units: Subjects | | | |
| Genotype 3 (No Confirmed Subtype) | 9 | 18 | 27 |
| Genotype 3a | 265 | 250 | 515 |
| Genotype 3b | 2 | 5 | 7 |
| Genotype 3h | 0 | 2 | 2 |
| Genotype 3k | 1 | 0 | 1 |
| Cirrhosis Status Units: Subjects | | | |
| Yes | 80 | 83 | 163 |
| No | 197 | 187 | 384 |
| Missing | 0 | 5 | 5 |

| | | | |
|---|--------|--------|-----|
| IL28b Status | | | |
| The CC, CT, and TT alleles are different forms of the IL28b gene. | | | |
| Units: Subjects | | | |
| CC | 105 | 111 | 216 |
| CT | 148 | 133 | 281 |
| TT | 24 | 31 | 55 |
| HCV RNA Category | | | |
| Units: Subjects | | | |
| < 800,000 IU/mL | 86 | 81 | 167 |
| ≥ 800,000 IU/mL | 191 | 194 | 385 |
| Prior HCV Treatment Experience | | | |
| Units: Subjects | | | |
| Treatment-Naive | 206 | 204 | 410 |
| Treatment-Experienced | 71 | 71 | 142 |
| HCV RNA | | | |
| Units: log10 IU/mL | | | |
| arithmetic mean | 6.2 | 6.3 | |
| standard deviation | ± 0.72 | ± 0.71 | - |

End points

End points reporting groups

| | |
|--|------------------|
| Reporting group title | SOF/VEL 12 Weeks |
| Reporting group description: SOF/VEL for 12 weeks | |
| Reporting group title | SOF+RBV 24 Weeks |
| Reporting group description: SOF+RBV for 24 weeks | |

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

| | |
|---|--|
| End point title | Percentage of Participants With Sustained Virologic Response (SVR) 12 Weeks After Discontinuation of Therapy (SVR12) |
| End point description: SVR12 was defined as HCV RNA < the lower limit of quantitation (LLOQ; ie, 15 IU/mL) at 12 weeks after stopping study treatment. Full Analysis Set: participants who were randomized into the study and received at least 1 dose of study drug. | |
| End point type | Primary |
| End point timeframe: Posttreatment Week 12 | |

| End point values | SOF/VEL 12 Weeks | SOF+RBV 24 Weeks | | |
|-----------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 277 | 275 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 95.3 (92.1 to 97.5) | 80.7 (75.6 to 85.2) | | |

Statistical analyses

| | |
|---|-------------------------------------|
| Statistical analysis title | Non-Inferiority Analysis - SVR12 |
| Statistical analysis description: Primary analyses consisted of non-inferiority test of Group 1 (SOF/VEL 12 weeks) versus Group 2 (SOF+RBV 24 weeks) at the 0.05 significance level. Non-inferiority was assessed using the conventional confidence interval approach and a non-inferiority margin of 10% was applied. The two-sided 95% confidence intervals was constructed using stratum-adjusted Mantel-Haenszel proportions, stratified by the randomization stratification factors (i.e cirrhosis status and prior treatment experience) | |
| Comparison groups | SOF/VEL 12 Weeks v SOF+RBV 24 Weeks |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 552 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[1] |
| Parameter estimate | Difference in proportions |
| Point estimate | 14.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 9.2 |
| upper limit | 19.6 |

Notes:

[1] - Difference in proportions between treatment groups and associated 95% confidence intervals (CI) are calculated based on stratum-adjusted Mantel-Haenszel proportions.

| | |
|-----------------------------------|------------------------------|
| Statistical analysis title | Superiority Analysis - SVR12 |
|-----------------------------------|------------------------------|

Statistical analysis description:

If the lower bound of 95% CI on the difference was > -10%, the p-value tested for the superiority of SOF/VEL for 12 weeks over SOF+RBV for 24 weeks. Superiority was demonstrated if the two-sided p-value is less than 0.05.

| | |
|---|-------------------------------------|
| Comparison groups | SOF/VEL 12 Weeks v SOF+RBV 24 Weeks |
| Number of subjects included in analysis | 552 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 ^[2] |
| Method | Cochran-Mantel-Haenszel |

Notes:

[2] - P-value was from the Cochran-Mantel-Haenszel test stratified by cirrhosis status and prior HCV treatment experience.

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 ^[3] |
|-----------------|---|

End point description:

Safety Analysis Set: participants who were randomized into the study and received at least 1 dose of study drug.

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

End point timeframe:

Up to 24 weeks

Notes:

[3] - 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 12 Weeks | SOF+RBV 24 Weeks | | |
|-----------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 277 | 275 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 0 | 3.3 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With SVR at 4 and 24 Weeks After Discontinuation of Therapy (SVR4 and SVR24)

| | |
|-----------------|---|
| End point title | Percentage of Participants With SVR at 4 and 24 Weeks After Discontinuation of Therapy (SVR4 and SVR24) |
|-----------------|---|

End point description:

SVR4 and SVR24 are defined as HCV RNA < LLOQ at 4 and 24 weeks following the last dose of study drug.

Full Analysis Set: participants who were randomized into the study and received at least 1 dose of study drug.

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

End point timeframe:

Posttreatment Weeks 4 and 24

| End point values | SOF/VEL 12 Weeks | SOF+RBV 24 Weeks | | |
|-----------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 277 | 275 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| SVR4 | 96.8 (93.9 to 98.5) | 82.2 (77.1 to 86.5) | | |
| SVR24 | 95.3 (92.1 to 97.5) | 80.7 (75.6 to 85.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HCV RNA < LLOQ at Weeks 1, 2, 4, 6, 8, 10, 12, 16, 20, and 24

| | |
|-----------------|---|
| End point title | Percentage of Participants With HCV RNA < LLOQ at Weeks 1, 2, 4, 6, 8, 10, 12, 16, 20, and 24 |
|-----------------|---|

End point description:

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

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

End point timeframe:

Weeks 1, 2, 4, 6, 8, 10, 12, 16, 20, and 24

| End point values | SOF/VEL 12 Weeks | SOF+RBV 24 Weeks | | |
|--|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 277 ^[4] | 275 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Week 1 (SOF/VEL: N = 277; SOF+RBV: N = 275) | 18.4 (14 to 23.5) | 17.5 (13.2 to 22.5) | | |
| Week 2 (SOF/VEL: N = 276; SOF+RBV: N = 274) | 62 (55.9 to 67.7) | 50 (43.9 to 56.1) | | |
| Week 4 (SOF/VEL: N = 276; SOF+RBV: N = 272) | 91.7 (87.8 to 94.6) | 88.2 (83.8 to 91.8) | | |
| Week 6 (SOF/VEL: N = 276; SOF+RBV: N = 269) | 96.7 (93.9 to 98.5) | 98.9 (96.8 to 99.8) | | |
| Week 8 (SOF/VEL: N = 276; SOF+RBV: N = 269) | 99.6 (98 to 100) | 99.3 (97.3 to 99.9) | | |
| Week 10 (SOF/VEL: N = 276; SOF+RBV: N = 268) | 100 (98.7 to 100) | 99.3 (97.3 to 99.9) | | |
| Week 12 (SOF/VEL: N = 275; SOF+RBV: N = 265) | 100 (98.7 to 100) | 99.6 (97.9 to 100) | | |
| Week 16 (SOF/VEL: N = 0; SOF+RBV: N = 262) | 9999 (9999 to 9999) | 98.9 (96.7 to 99.8) | | |
| Week 20 (SOF/VEL: N = 0; SOF+RBV: N = 260) | 9999 (9999 to 9999) | 99.6 (97.9 to 100) | | |
| Week 24 (SOF/VEL: N = 0; SOF+RBV: N = 255) | 9999 (9999 to 9999) | 100 (98.6 to 100) | | |

Notes:

[4] - 9999 = Not applicable; Participants in the SOF/VEL group were only treated for 12 weeks.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in HCV RNA at Weeks 1, 2, 4, 6, 8, 10, 12, 16, 20, and 24

| | |
|--|--|
| End point title | Change From Baseline in HCV RNA at Weeks 1, 2, 4, 6, 8, 10, 12, 16, 20, and 24 |
| End point description: | |
| Participants in the Full Analysis Set with available data were analyzed. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline; Weeks 1, 2, 4, 6, 8, 10, 12, 16, 20, and 24 | |

| End point values | SOF/VEL 12 Weeks | SOF+RBV 24 Weeks | | |
|---|--------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 277 ^[5] | 275 | | |
| Units: log10 IU/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Wk 1 (SOF/VEL: N =272; SOF+RBV: N =268) | -4.26 (± 0.644) | -4.16 (± 0.64) | | |
| Change at Wk 2 (SOF/VEL: N =274; SOF+RBV: N =272) | -4.82 (± 0.769) | -4.79 (± 0.702) | | |

| | | | | |
|---|--------------------|--------------------|--|--|
| Change at Wk 4 (SOF/VEL: N =276; SOF+RBV: N =270) | -5.02 (± 0.776) | -5.09 (± 0.699) | | |
| Change at Wk 6 (SOF/VEL: N =275; SOF+RBV: N =269) | -5.06 (± 0.718) | -5.13 (± 0.712) | | |
| Change at Wk 8 (SOF/VEL: N =276; SOF+RBV: N =269) | -5.07 (± 0.728) | -5.13 (± 0.712) | | |
| Change at Wk 10 (SOF/VEL: N =276; SOF+RBV: N =267) | -5.07 (± 0.723) | -5.14 (± 0.71) | | |
| Change at Wk 12 (SOF/VEL: N =275; SOF+RBV: N =264) | -5.08 (± 0.721) | -5.14 (± 0.711) | | |
| Change at Wk 16 (SOF/VEL: N = 0; SOF+RBV: N = 262) | 9999 (± 9999) | -5.11 (± 0.765) | | |
| Change at Wk 20 (SOF/VEL: N = 0; SOF+RBV: N = 259) | 9999 (± 9999) | -5.14 (± 0.715) | | |
| Change at Wk 24 (SOF/VEL: N = 0; SOF+RBV: N = 255) | 9999 (± 9999) | -5.14 (± 0.715) | | |

Notes:

[5] - 9999 = Not applicable; Participants in the SOF/VEL group were only treated for 12 weeks.

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 \geq LLOQ after having previously had HCV RNA $<$ LLOQ 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 \geq LLOQ through 8 weeks of treatment)
- Virologic relapse:
 - Confirmed HCV RNA \geq LLOQ during the posttreatment period having achieved HCV RNA $<$ LLOQ at last on-treatment visit.

Full Analysis Set: participants who were randomized into the study and received at least 1 dose of study drug.

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

End point timeframe:

Up to Posttreatment Week 24

| End point values | SOF/VEL 12 Weeks | SOF+RBV 24 Weeks | | |
|-----------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 277 | 275 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 4 | 14.2 | | |

Statistical analyses

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 24 weeks plus 30 days

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

Dictionary used

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

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

Reporting groups

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

Reporting group description:

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

| | |
|-----------------------|------------------|
| Reporting group title | SOF+RBV 24 Weeks |
|-----------------------|------------------|

Reporting group description:

SOF 400 mg tablet once daily + RBV tablets (1000 or 1200 mg daily based on weight) for 24 weeks

| Serious adverse events | SOF/VEL 12 Weeks | SOF+RBV 24 Weeks | |
|--|------------------|------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 277 (2.17%) | 15 / 275 (5.45%) | |
| number of deaths (all causes) | 0 | 2 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Vascular disorders | | | |
| Peripheral artery stenosis | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 1 / 275 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Death | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 1 / 275 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Reproductive system and breast disorders | | | |
| Ovarian cyst ruptured | | | |
| subjects affected / exposed | 1 / 277 (0.36%) | 0 / 275 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal | | | |

| | | | |
|---|-----------------|-----------------|--|
| disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 1 / 275 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 1 / 275 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychotic disorder | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 1 / 275 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Forearm fracture | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 1 / 275 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gun shot wound | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 1 / 275 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Intentional overdose | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 1 / 275 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 277 (0.36%) | 0 / 275 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 277 (0.00%) | 1 / 275 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intracranial aneurysm | | | |
| subjects affected / exposed | 1 / 277 (0.36%) | 0 / 275 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ruptured cerebral aneurysm | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 1 / 275 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Food poisoning | | | |
| subjects affected / exposed | 1 / 277 (0.36%) | 0 / 275 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematochezia | | | |
| subjects affected / exposed | 1 / 277 (0.36%) | 0 / 275 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 1 / 277 (0.36%) | 0 / 275 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 1 / 275 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Bursitis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 277 (0.00%) | 1 / 275 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 1 / 275 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 1 / 275 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung infection | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 1 / 275 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Propionibacterium infection | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 1 / 275 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | SOF/VEL 12 Weeks | SOF+RBV 24 Weeks | |
|---|--------------------|--------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 216 / 277 (77.98%) | 243 / 275 (88.36%) | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 90 / 277 (32.49%) | 90 / 275 (32.73%) | |
| occurrences (all) | 111 | 114 | |
| Dizziness | | | |
| subjects affected / exposed | 15 / 277 (5.42%) | 21 / 275 (7.64%) | |
| occurrences (all) | 15 | 23 | |
| Disturbance in attention | | | |

| | | | |
|--|--|--|--|
| subjects affected / exposed occurrences (all) | 7 / 277 (2.53%) 7 | 14 / 275 (5.09%) 14 | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 1 / 277 (0.36%) 1 | 25 / 275 (9.09%) 25 | |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) | 71 / 277 (25.63%) 73 4 / 277 (1.44%) 4 | 105 / 275 (38.18%) 107 14 / 275 (5.09%) 15 | |
| Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Asthenia subjects affected / exposed occurrences (all) | 47 / 277 (16.97%) 49 9 / 277 (3.25%) 10 20 / 277 (7.22%) 21 10 / 277 (3.61%) 10 13 / 277 (4.69%) 13 8 / 277 (2.89%) 9 16 / 277 (5.78%) 16 | 58 / 275 (21.09%) 69 30 / 275 (10.91%) 33 21 / 275 (7.64%) 22 19 / 275 (6.91%) 21 21 / 275 (7.64%) 21 20 / 275 (7.27%) 26 26 / 275 (9.45%) 28 | |
| Reproductive system and breast disorders | | | |

| | | | |
|---|-------------------------|-------------------------|--|
| Cough subjects affected / exposed occurrences (all) | 14 / 277 (5.05%) 15 | 35 / 275 (12.73%) 39 | |
| Dyspnoea exertional subjects affected / exposed occurrences (all) | 3 / 277 (1.08%) 3 | 20 / 275 (7.27%) 20 | |
| Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all) | 8 / 277 (2.89%) 9 | 22 / 275 (8.00%) 22 | |
| Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) | 8 / 277 (2.89%) 8 | 35 / 275 (12.73%) 36 | |
| Rash subjects affected / exposed occurrences (all) | 15 / 277 (5.42%) 15 | 14 / 275 (5.09%) 18 | |
| Dry skin subjects affected / exposed occurrences (all) | 2 / 277 (0.72%) 2 | 25 / 275 (9.09%) 25 | |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) | 32 / 277 (11.55%) 32 | 74 / 275 (26.91%) 81 | |
| Irritability subjects affected / exposed occurrences (all) | 23 / 277 (8.30%) 23 | 40 / 275 (14.55%) 41 | |
| Anxiety subjects affected / exposed occurrences (all) | 7 / 277 (2.53%) 8 | 21 / 275 (7.64%) 21 | |
| Sleep disorder subjects affected / exposed occurrences (all) | 9 / 277 (3.25%) 9 | 15 / 275 (5.45%) 18 | |
| Musculoskeletal and connective tissue disorders Back pain | | | |

| | | | |
|------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed | 25 / 277 (9.03%) | 20 / 275 (7.27%) | |
| occurrences (all) | 27 | 22 | |
| Arthralgia | | | |
| subjects affected / exposed | 10 / 277 (3.61%) | 22 / 275 (8.00%) | |
| occurrences (all) | 14 | 22 | |
| Muscle spasms | | | |
| subjects affected / exposed | 13 / 277 (4.69%) | 17 / 275 (6.18%) | |
| occurrences (all) | 15 | 18 | |
| Myalgia | | | |
| subjects affected / exposed | 10 / 277 (3.61%) | 15 / 275 (5.45%) | |
| occurrences (all) | 10 | 15 | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 34 / 277 (12.27%) | 33 / 275 (12.00%) | |
| occurrences (all) | 38 | 37 | |
| Bronchitis | | | |
| subjects affected / exposed | 6 / 277 (2.17%) | 14 / 275 (5.09%) | |
| occurrences (all) | 6 | 14 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 8 / 277 (2.89%) | 14 / 275 (5.09%) | |
| occurrences (all) | 8 | 14 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 23 February 2015 | Subjects randomized to Group 2 will not be enrolled into either the SVR or the Sequence registries |

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:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/26575258>