



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

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