

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	
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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	

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:	-
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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 on	ce 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 $\ge 75 \text{ kg} = 1200 \text{ mg}$)

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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

^{[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	49	50	
standard deviation	± 10.4	± 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	1		
Black or African American	3	1	4
White	250	239	489
Asian	23	29	52
American Indian or Alaska Native	1	3	4
Native Hawai	\	·	•

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IL28b Status			
The CC, CT, and TT alleles are different forms of the IL28b gene.			
Units: Subjects			
СС	105	111	216
ст	148	133	281
π	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	

EU-CTR publication date: 11 November 2016

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

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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

[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
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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:

 ${\sf SVR4}$ and ${\sf SVR24}$ are defined as ${\sf HCV}$ ${\sf RNA}$ < ${\sf LLOQ}$ 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

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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)	

[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)	

[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 ≥ 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 ≥ LLOQ through 8 weeks of treatment)
- Virologic relapse:
- •• Confirmed HCV RNA ≥ LLOQ during the posttreatment period having achieved HCV RNA < LLOQ at last ontreatment 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

No statistical analyses	for this end point		
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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 tabl	et 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	7		
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			
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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	1		
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	7 / 277 (2.53%)	14 / 275 (5.09%)	
occurrences (all)	7	14	
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed	1 / 277 (0.36%)	25 / 275 (9.09%)	
occurrences (all)	1	25 273 (9.09 70)	
Coccurrences (an)	1	23	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	71 / 277 (25.63%)	105 / 275 (38.18%)	
occurrences (all)	73	107	
Pyrexia			
subjects affected / exposed	4 / 277 (1.44%)	14 / 275 (5.09%)	
occurrences (all)			
occurrences (an)	4	15	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	47 / 277 (16.97%)	58 / 275 (21.09%)	
occurrences (all)	49	69	
Dyspepsia			
subjects affected / exposed	9 / 277 (3.25%)	30 / 275 (10.91%)	
occurrences (all)	10	33	
		33	
Diarrhoea			
subjects affected / exposed	20 / 277 (7.22%)	21 / 275 (7.64%)	
occurrences (all)	21	22	
Abdominal pain			
subjects affected / exposed	10 / 277 /2 610/	10 / 275 /6 010/ \	
	10 / 277 (3.61%)	19 / 275 (6.91%)	
occurrences (all)	10	21	
Constipation			
subjects affected / exposed	13 / 277 (4.69%)	21 / 275 (7.64%)	
occurrences (all)	13	21	
Vomiting			
subjects affected / exposed	8 / 277 (2.89%)	20 / 275 (7.27%)	
occurrences (all)	9	26	
Asthenia			
subjects affected / exposed	16 / 277 (5.78%)	26 / 275 (9.45%)	
occurrences (all)	16	28	
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Reproductive system and breast disorders			
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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	
occurrences (un)	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	
occurrences (un)	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.

EU-CTR publication date: 11 November 2016

There were no limitations affecting the analysis or results.

Notes:

Online references

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