Clinical trial results:
A Phase 3B Randomized, Open-Label, Multi-Center Trial Assessing Sofosbuvir + Ribavirin for 16 or 24 Weeks and Sofosbuvir + Pegylated Interferon + Ribavirin for 12 Weeks in Subjects with Genotype 2 or 3 Chronic HCV Infection

Summary

EudraCT number	2013-002641-11
Trial protocol	GB
Global end of trial date	07 July 2016

Results information

Result version number	v1 (current)
This version publication date	06 July 2017
First version publication date	06 July 2017

Trial information

Trial identification

Sponsor protocol code	GS-US-334-0153

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01962441
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 Trials Mailbox, Gilead Sciences International Ltd, ClinicalTrialDisclosures@gilead.com
Scientific contact	Clinical Trials 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	07 July 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 July 2016
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 determine the efficacy of sofosbuvir (SOF) + ribavirin (RBV) for 16 or 24 weeks as measured by the proportion of participants with sustained viral response 12 weeks after discontinuation of treatment (SVR12)
- To determine the efficacy of SOF+RBV+pegylated interferon alfa 2a (Peg-IFN) for 12 weeks as measured by the proportion of participants with SVR12
- To evaluate the safety and tolerability of all 3 treatment arms as assessed by review of the accumulated safety data.

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	23 September 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 254
Country: Number of subjects enrolled	Australia: 128
Country: Number of subjects enrolled	United States: 93
Country: Number of subjects enrolled	Canada: 84
Country: Number of subjects enrolled	New Zealand: 42
Worldwide total number of subjects	601
EEA total number of subjects	254

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)	570
From 65 to 84 years	31
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Europe, North America, Australia, and New Zealand. The first participant was screened on 24 September 2013. The last study visit occurred on 07 July 2016.

Pre-assignment

Screening details:

776 participants were screened.

Period 1

Period 1 title	Randomized Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	SOF+RBV 16 Weeks

Arm description:

Randomized Period: Sofosbuvir (Sovaldi®; SOF) + ribavirin (RBV) for 16 weeks

Arm type	Experimental
Investigational medicinal product name	Sofosbuvir
Investigational medicinal product code	
Other name	SOF, 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	RBV
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)

Arm title	SOF+RBV 24 Weeks

Arm description:

Randomized Period: SOF+RBV 24 weeks

Arm type	Experimental
Investigational medicinal product name	Sofosbuvir
Investigational medicinal product code	
Other name	SOF, 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	RBV

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)

Arm title	SOF+RBV+Peg-IFN 12 Weeks

Arm description:

Randomized Period: SOF+RBV + pegylated interferon (Peg-IFN) for 12 weeks.

Participants in this group were not eligible to enroll into the Retreatment Period.

Arm type	Experimental
Investigational medicinal product name	Sofosbuvir
Investigational medicinal product code	
Other name	SOF, 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	RBV
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)

Investigational medicinal product name	Pegylated interferon
Investigational medicinal product code	
Other name	Peg-IFN
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

180 µg administered once weekly

Number of subjects in period 1[1]	SOF+RBV 16 Weeks	SOF+RBV 24 Weeks	SOF+RBV+Peg-IFN 12 Weeks
Started	196	199	197
Completed	190	190	189
Not completed	6	9	8
Withdrew Consent	3	3	2
Adverse event, non-fatal	1	1	-
Death	-	-	2
Protocol Violation	-	1	-
Lost to follow-up	2	4	4

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: 9 participants who were randomized but never treated are not included in the subject disposition table.

Period 2

Period 2 title	Retreatment Substudy
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	SOF+RBV 16 Weeks, Then Retreatment with SOF+Peg-IFN+RBV 12 Wks

Arm description:

Retreatment Period: Participants who experienced virologic failure during treatment or relapsed at or before Posttreatment Week 24 during the Randomized Period were eligible to enroll into the Retreatment Period to receive SOF+Peg-IFN+RBV for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Sofosbuvir
Investigational medicinal product code	
Other name	SOF, 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	RBV
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)

Investigational medicinal product name	Pegylated interferon
Investigational medicinal product code	
Other name	Peg-IFN
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

180 µg administered once weekly

Arm title	SOF+RBV 24 Weeks, Then Retreatment with SOF+Peg-IFN+RBV 12 Wks

Arm description:

Retreatment Period: Participants who experienced virologic failure during treatment or relapsed at or before Posttreatment Week 24 during the Randomized Period were eligible to enroll into the Retreatment Period to receive SOF+Peg-IFN+RBV for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Sofosbuvir
Investigational medicinal product code	
Other name	SOF, 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	RBV
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)	
Investigational medicinal product name	Pegylated interferon
Investigational medicinal product code	
Other name	Peg-IFN
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details: 180 µg administered once weekly	

Number of subjects in period 2[2]	SOF+RBV 16 Weeks, Then Retreatment with SOF+Peg-IFN+RBV 12 Wks	SOF+RBV 24 Weeks, Then Retreatment with SOF+Peg-IFN+RBV 12 Wks
Started	20	10
Completed	18	10
Not completed	2	0
Lost to follow-up	1	-
Lack of efficacy	1	-

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: 30 participants who experienced virologic failure enrolled into the Retreatment Substudy.

Baseline characteristics

Reporting groups	
Reporting group title	SOF+RBV 16 Weeks
Reporting group description:	
Randomized Period: Sofosbuvir (Sovaldi®; SOF) + ribavirin (RBV) for 16 weeks	
Reporting group title	SOF+RBV 24 Weeks
Reporting group description:	
Randomized Period: SOF+RBV 24 weeks	
Reporting group title	SOF+RBV+Peg-IFN 12 Weeks
Reporting group description:	
Randomized Period: SOF+RBV + pegylated interferon (Peg-IFN) for 12 weeks. Participants in this group were not eligible to enroll into the Retreatment Period.	

Reporting group values	SOF+RBV 16 Weeks	SOF+RBV 24 Weeks	SOF+RBV+Peg-IFN 12 Weeks
Number of subjects	196	199	197
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	51	49	50
standard deviation	± 9.7	± 9.8	± 10.2
Gender categorical Units: Subjects			
Female	62	70	65
Male	134	129	132
Ethnicity Units: Subjects			
Hispanic or Latino	5	5	2
Not Hispanic or Latino	188	188	191
Not Disclosed	3	6	4
Race Units: Subjects			
Black or African American	2	2	2
White	162	168	165
Asian	29	26	25
American Indian/ Alaska Native/ First Nations	2	0	0
Hawaiian or Pacific Islander	0	1	2
Other	0	1	1
Not Disclosed	1	1	2
HCV Genotype Units: Subjects			
Genotype 2	15	17	16
Genotype 3	181	182	181
IL28b Status			
CC, CT, and TT alleles are different forms of the IL28b gene.			

Units: Subjects			
CC	75	73	78
CT	94	95	98
TT	27	31	21
HCV RNA Category Units: Subjects			
< 6 log10 IU/mL	60	72	60
≥ 6 log10 IU/mL	136	127	137
HCV RNA Units: log10 IU/mL			
arithmetic mean	6.3	6.2	6.3
standard deviation	± 0.68	± 0.71	± 0.69

Reporting group values	Total		
Number of subjects	592		
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Female	197		
Male	395		
Ethnicity Units: Subjects			
Hispanic or Latino	12		
Not Hispanic or Latino	567		
Not Disclosed	13		
Race Units: Subjects			
Black or African American	6		
White	495		
Asian	80		
American Indian/ Alaska Native/ First Nations	2		
Hawaiian or Pacific Islander	3		
Other	2		
Not Disclosed	4		
HCV Genotype Units: Subjects			
Genotype 2	48		
Genotype 3	544		
IL28b Status			
CC, CT, and TT alleles are different forms of the IL28b gene.			
Units: Subjects			
CC	226		
CT	287		
TT	79		

HCV RNA Category Units: Subjects			
< 6 log10 IU/mL	192		
≥ 6 log10 IU/mL	400		
HCV RNA Units: log10 IU/mL arithmetic mean standard deviation	- -		

End points

End points reporting groups

Reporting group title	SOF+RBV 16 Weeks
Reporting group description:	
Randomized Period: Sofosbuvir (Sovaldi®; SOF) + ribavirin (RBV) for 16 weeks	
Reporting group title	SOF+RBV 24 Weeks
Reporting group description:	
Randomized Period: SOF+RBV 24 weeks	
Reporting group title	SOF+RBV+Peg-IFN 12 Weeks
Reporting group description:	
Randomized Period: SOF+RBV + pegylated interferon (Peg-IFN) for 12 weeks. Participants in this group were not eligible to enroll into the Retreatment Period.	
Reporting group title	SOF+RBV 16 Weeks, Then Retreatment with SOF+Peg-IFN+RBV 12 Wks
Reporting group description:	
Retreatment Period: Participants who experienced virologic failure during treatment or relapsed at or before Posttreatment Week 24 during the Randomized Period were eligible to enroll into the Retreatment Period to receive SOF+Peg-IFN+RBV for 12 weeks.	
Reporting group title	SOF+RBV 24 Weeks, Then Retreatment with SOF+Peg-IFN+RBV 12 Wks
Reporting group description:	
Retreatment Period: Participants who experienced virologic failure during treatment or relapsed at or before Posttreatment Week 24 during the Randomized Period were eligible to enroll into the Retreatment Period to receive SOF+Peg-IFN+RBV for 12 weeks.	
Subject analysis set title	SOF+RBV 16 Weeks
Subject analysis set type	Full analysis
Subject analysis set description:	
SOF+RBV for 16 weeks	
Subject analysis set title	SOF+RBV 24 Weeks
Subject analysis set type	Full analysis
Subject analysis set description:	
SOF+RBV for 24 weeks	
Subject analysis set title	SOF+RBV+Peg-IFN 12 Weeks
Subject analysis set type	Full analysis
Subject analysis set description:	
SOF+RBV+Peg-IFN for 12 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)[1]
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 with genotype 2 or 3 HCV infection who were randomized and received at least 1 dose of study drug.	
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+RBV 16 Weeks	SOF+RBV 24 Weeks	SOF+RBV+Peg -IFN 12 Weeks	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	196	199	197	
Units: percentage of participants				
number (not applicable)	71.9	85.4	92.9	

Statistical analyses

No statistical analyses for this end point

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[2]

End point description:

Safety Analysis Set: participants with genotype 2 or 3 HCV infection who were randomized and received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

Up to 24 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+RBV 16 Weeks	SOF+RBV 24 Weeks	SOF+RBV+Peg -IFN 12 Weeks	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	196	199	197	
Units: percentage of participants				
number (not applicable)	1.5	1.5	1.5	

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 SVR 24 were defined as HCV RNA < LLOQ at 4 and 24 weeks after stopping study treatment, respectively.

Full Analysis Set: participants with genotype 2 or 3 HCV infection who were randomized 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+RBV 16 Weeks	SOF+RBV 24 Weeks	SOF+RBV+Peg -IFN 12 Weeks	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	196	199	197	
Units: percentage of participants				
number (not applicable)				
SVR4	73	85.9	95.9	
SVR24	71.9	84.4	93.4	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Full Analysis Set: participants with genotype 2 or 3 HCV infection who were randomized and received at least 1 dose of study drug.

9999 = NA; Treatment for these groups was only 12 or 16 weeks.

End point type	Secondary

End point timeframe:

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

End point values	SOF+RBV 16 Weeks	SOF+RBV 24 Weeks	SOF+RBV+Peg -IFN 12 Weeks	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	196	199	197	
Units: percentage of participants				
number (not applicable)				
Wk 1 (16 Wk: n=196; 24 Wk: n=199; 12 Wk: n=197)	14.8	20.1	25.9	
Wk 2 (16 Wk: n=195; 24 Wk: n=198; 12 Wk: n=197)	53.3	53.5	67	
Wk 4 (16 Wk: n=194; 24 Wk: n=198; 12 Wk: n=195)	86.6	91.9	97.4	
Wk 8 (16 Wk: n=193; 24 Wk: n=198; 12 Wk: n=195)	99.5	99.5	99.5	

Wk 12 (16 Wk: n=190; 24 Wk: n=197; 12 Wk: n=194)	100	98.5	100	
Wk 16 (16 Wk: n=191; 24 Wk: n=194)	99	99.5	9999	
Wk 20 (24 Wk: n=194)	9999	99.5	9999	
Wk 24 (24 Wk: n=193)	9999	100	9999	

Statistical analyses

No statistical analyses for this end point

Secondary: HCV RNA at Weeks 1, 2, 4, 8, and 12

End point title	HCV RNA at Weeks 1, 2, 4, 8, and 12
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, 8, and 12	

End point values	SOF+RBV 16 Weeks	SOF+RBV 24 Weeks	SOF+RBV+Peg -IFN 12 Weeks	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	196	199	197	
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Wk 1 (16 Wk: n=194; 24 Wk: n=197; 12 Wk: n=194)	2.13 (± 0.658)	2.08 (± 0.749)	1.81 (± 0.576)	
Wk 2 (16 Wk: n=191; 24 Wk: n=196; 12 Wk: n=195)	1.44 (± 0.436)	1.45 (± 0.487)	1.32 (± 0.342)	
Wk 4 (16 Wk: n=193; 24 Wk: n=198; 12 Wk: n=195)	1.19 (± 0.156)	1.21 (± 0.287)	1.16 (± 0)	
Wk 8 (16 Wk: n=193; 24 Wk: n=198; 12 Wk: n=194)	1.15 (± 0.021)	1.15 (± 0.1)	1.15 (± 0)	
Wk 12 (16 Wk: n=191; 24 Wk: n=197; 12 Wk: n=194)	1.15 (± 0)	1.17 (± 0.318)	1.15 (± 0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in HCV RNA at Weeks 1, 2, 4, 8, and 12

End point title	Change From Baseline in HCV RNA at Weeks 1, 2, 4, 8, and 12
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, 8, and 12	

End point values	SOF+RBV 16 Weeks	SOF+RBV 24 Weeks	SOF+RBV+Peg -IFN 12 Weeks	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	196	199	197	
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Wk 1 (16 Wk: n=194; 24 Wk: n=197; 12 Wk: n=194)	-4.18 (± 0.559)	-4.15 (± 0.664)	-4.46 (± 0.556)	
Wk 2 (16 Wk: n=191; 24 Wk: n=196; 12 Wk: n=195)	-4.86 (± 0.661)	-4.78 (± 0.714)	-4.96 (± 0.661)	
Wk 4 (16 Wk: n=193; 24 Wk: n=198; 12 Wk: n=195)	-5.11 (± 0.671)	-5.02 (± 0.735)	-5.12 (± 0.699)	
Wk 8 (16 Wk: n=193; 24 Wk: n=198; 12 Wk: n=194)	-5.16 (± 0.684)	-5.08 (± 0.708)	-5.12 (± 0.691)	
Wk 12 (16 Wk: n=191; 24 Wk: n=197; 12 Wk: n=194)	-5.15 (± 0.686)	-5.05 (± 0.788)	-5.12 (± 0.691)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing On-Treatment Virologic Failure

End point title	Percentage of Participants Experiencing On-Treatment Virologic Failure

End point description:

On-treatment virologic failure was defined as:
• 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)

End point type	Secondary

End point timeframe:

Up to 24 weeks

End point values	SOF+RBV 16 Weeks	SOF+RBV 24 Weeks	SOF+RBV+Peg -IFN 12 Weeks	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	196	199	197	
Units: percentage of participants				
number (not applicable)	0	1.5	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing Viral Relapse

End point title	Percentage of Participants Experiencing Viral Relapse

End point description:

Viral relapse is defined as 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 with available data were analyzed.

End point type	Secondary

End point timeframe:

Up to Posttreatment Week 24

End point values	SOF+RBV 16 Weeks	SOF+RBV 24 Weeks	SOF+RBV+Peg -IFN 12 Weeks	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	195	195	195	
Units: percentage of participants				
number (not applicable)	26.7	12.3	4.6	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 24 weeks plus 30 days (Randomized Period); Up to 12 additional weeks plus 30 days (Retreatment Period)

Adverse event reporting additional description:

Safety Analysis Set: participants with genotype 2 or 3 HCV infection who were randomized and received at least 1 dose of study drug.

MedDRA version 18.0 = Randomized Period; MedDRA version 19.0 = Retreatment Period

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0, 19.0

Reporting groups

Reporting group title	Randomized Period: SOF+RBV 16 Weeks

Reporting group description:

Randomized Period: SOF+RBV for 16 weeks

Reporting group title	Randomized Period: SOF+RBV 24 Weeks

Reporting group description:

Randomized Period: SOF+RBV 24 weeks

Reporting group title	Randomized Period: SOF+RBV+Peg-IFN 12 Weeks

Reporting group description:

Randomized Period: SOF+RBV+Peg-IFN for 12 weeks.

Reporting group title	Retreatment Period: SOF+RBV+Peg- IFN 12 Weeks

Reporting group description:

Retreatment Period: Participants from the SOF+RBV 16 Weeks or 24 Weeks groups who experienced virologic failure during treatment or relapsed at or before Posttreatment Week 24 during the Randomized Period were eligible to enroll into the Retreatment Period to receive SOF+RBV+Peg-IFN for 12 weeks.

Serious adverse events	Randomized Period: SOF+RBV 16 Weeks	Randomized Period: SOF+RBV 24 Weeks	Randomized Period: SOF+RBV+Peg-IFN 12 Weeks
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 196 (4.08%)	10 / 199 (5.03%)	12 / 197 (6.09%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 196 (0.51%)	0 / 199 (0.00%)	0 / 197 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatocellular carcinoma			

subjects affected / exposed	0 / 196 (0.00%)	1 / 199 (0.50%)	0 / 197 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	1 / 196 (0.51%)	0 / 199 (0.00%)	0 / 197 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 196 (0.51%)	0 / 199 (0.00%)	0 / 197 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Miscarriage of partner			
subjects affected / exposed	0 / 196 (0.00%)	1 / 199 (0.50%)	0 / 197 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pleuritic pain			
subjects affected / exposed	0 / 196 (0.00%)	0 / 199 (0.00%)	1 / 197 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	0 / 196 (0.00%)	1 / 199 (0.50%)	0 / 197 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alcohol withdrawal syndrome			
subjects affected / exposed	0 / 196 (0.00%)	0 / 199 (0.00%)	1 / 197 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			

subjects affected / exposed	1 / 196 (0.51%)	0 / 199 (0.00%)	1 / 197 (0.51%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug abuse			
subjects affected / exposed	0 / 196 (0.00%)	1 / 199 (0.50%)	0 / 197 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination			
subjects affected / exposed	0 / 196 (0.00%)	0 / 199 (0.00%)	1 / 197 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	1 / 196 (0.51%)	0 / 199 (0.00%)	0 / 197 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Haemoglobin decreased			
subjects affected / exposed	0 / 196 (0.00%)	0 / 199 (0.00%)	1 / 197 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	0 / 196 (0.00%)	1 / 199 (0.50%)	0 / 197 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Snake bite			
subjects affected / exposed	0 / 196 (0.00%)	0 / 199 (0.00%)	1 / 197 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 196 (0.51%)	0 / 199 (0.00%)	0 / 197 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Atrial fibrillation			
subjects affected / exposed	0 / 196 (0.00%)	1 / 199 (0.50%)	1 / 197 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Loss of consciousness			
subjects affected / exposed	0 / 196 (0.00%)	0 / 199 (0.00%)	1 / 197 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 196 (0.00%)	1 / 199 (0.50%)	1 / 197 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 196 (0.00%)	1 / 199 (0.50%)	0 / 197 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 196 (0.00%)	0 / 199 (0.00%)	1 / 197 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 196 (0.51%)	1 / 199 (0.50%)	0 / 197 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 196 (0.00%)	0 / 199 (0.00%)	1 / 197 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthritis			

subjects affected / exposed	1 / 196 (0.51%)	0 / 199 (0.00%)	0 / 197 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flank pain			
subjects affected / exposed	0 / 196 (0.00%)	1 / 199 (0.50%)	0 / 197 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 196 (0.00%)	1 / 199 (0.50%)	0 / 197 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal pain			
subjects affected / exposed	0 / 196 (0.00%)	0 / 199 (0.00%)	0 / 197 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 196 (0.51%)	0 / 199 (0.00%)	0 / 197 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 196 (0.00%)	0 / 199 (0.00%)	1 / 197 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 196 (0.00%)	0 / 199 (0.00%)	1 / 197 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	0 / 196 (0.00%)	1 / 199 (0.50%)	0 / 197 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Retreatment Period:		

	SOF+RBV+Peg- IFN 12 Weeks		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 30 (3.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatocellular carcinoma			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Social circumstances			
Miscarriage of partner			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pleuritic pain			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Alcohol withdrawal syndrome			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Depression			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Drug abuse			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hallucination			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Suicidal ideation			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Haemoglobin decreased			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Overdose			

subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Snake bite			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Loss of consciousness			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Pancreatitis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Arthritis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Flank pain				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal chest pain				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal pain				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Cellulitis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Respiratory tract infection			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subcutaneous abscess			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Randomized Period: SOF+RBV 16 Weeks	Randomized Period: SOF+RBV 24 Weeks	Randomized Period: SOF+RBV+Peg-IFN 12 Weeks
Total subjects affected by non-serious adverse events			
subjects affected / exposed	173 / 196 (88.27%)	176 / 199 (88.44%)	192 / 197 (97.46%)
Investigations			
Platelet count decreased			
subjects affected / exposed	0 / 196 (0.00%)	0 / 199 (0.00%)	3 / 197 (1.52%)
occurrences (all)	0	0	3
Nervous system disorders			
Dizziness			
subjects affected / exposed	11 / 196 (5.61%)	16 / 199 (8.04%)	13 / 197 (6.60%)
occurrences (all)	11	17	14
Dizziness postural			
subjects affected / exposed	3 / 196 (1.53%)	1 / 199 (0.50%)	10 / 197 (5.08%)
occurrences (all)	3	1	10
Dysgeusia			
subjects affected / exposed	6 / 196 (3.06%)	4 / 199 (2.01%)	10 / 197 (5.08%)
occurrences (all)	6	4	11
Headache			
subjects affected / exposed	61 / 196 (31.12%)	72 / 199 (36.18%)	70 / 197 (35.53%)
occurrences (all)	65	86	78
Lethargy			
subjects affected / exposed	9 / 196 (4.59%)	8 / 199 (4.02%)	10 / 197 (5.08%)
occurrences (all)	9	8	10
Memory impairment			

subjects affected / exposed	10 / 196 (5.10%)	3 / 199 (1.51%)	5 / 197 (2.54%)
occurrences (all)	10	3	5
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 196 (2.04%)	7 / 199 (3.52%)	12 / 197 (6.09%)
occurrences (all)	4	9	12
Neutropenia			
subjects affected / exposed	0 / 196 (0.00%)	0 / 199 (0.00%)	11 / 197 (5.58%)
occurrences (all)	0	0	12
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 196 (1.02%)	3 / 199 (1.51%)	10 / 197 (5.08%)
occurrences (all)	2	3	10
Chills			
subjects affected / exposed	3 / 196 (1.53%)	4 / 199 (2.01%)	21 / 197 (10.66%)
occurrences (all)	3	4	21
Fatigue			
subjects affected / exposed	74 / 196 (37.76%)	83 / 199 (41.71%)	92 / 197 (46.70%)
occurrences (all)	78	86	92
Influenza like illness			
subjects affected / exposed	7 / 196 (3.57%)	8 / 199 (4.02%)	39 / 197 (19.80%)
occurrences (all)	7	10	42
Injection site rash			
subjects affected / exposed	0 / 196 (0.00%)	0 / 199 (0.00%)	5 / 197 (2.54%)
occurrences (all)	0	0	5
Pyrexia			
subjects affected / exposed	5 / 196 (2.55%)	7 / 199 (3.52%)	29 / 197 (14.72%)
occurrences (all)	5	8	32
Eye disorders			
Dry eye			
subjects affected / exposed	3 / 196 (1.53%)	5 / 199 (2.51%)	5 / 197 (2.54%)
occurrences (all)	3	5	5
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	8 / 196 (4.08%)	8 / 199 (4.02%)	11 / 197 (5.58%)
occurrences (all)	9	8	11

Abdominal pain upper			
subjects affected / exposed	7 / 196 (3.57%)	10 / 199 (5.03%)	9 / 197 (4.57%)
occurrences (all)	8	11	10
Diarrhoea			
subjects affected / exposed	21 / 196 (10.71%)	18 / 199 (9.05%)	27 / 197 (13.71%)
occurrences (all)	22	20	32
Dry mouth			
subjects affected / exposed	3 / 196 (1.53%)	7 / 199 (3.52%)	12 / 197 (6.09%)
occurrences (all)	3	7	12
Dyspepsia			
subjects affected / exposed	10 / 196 (5.10%)	12 / 199 (6.03%)	11 / 197 (5.58%)
occurrences (all)	12	12	11
Gastrooesophageal reflux disease			
subjects affected / exposed	4 / 196 (2.04%)	8 / 199 (4.02%)	3 / 197 (1.52%)
occurrences (all)	4	8	3
Mouth ulceration			
subjects affected / exposed	5 / 196 (2.55%)	3 / 199 (1.51%)	5 / 197 (2.54%)
occurrences (all)	5	4	5
Nausea			
subjects affected / exposed	32 / 196 (16.33%)	34 / 199 (17.09%)	50 / 197 (25.38%)
occurrences (all)	33	38	51
Vomiting			
subjects affected / exposed	10 / 196 (5.10%)	21 / 199 (10.55%)	19 / 197 (9.64%)
occurrences (all)	10	23	28
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	10 / 196 (5.10%)	19 / 199 (9.55%)	28 / 197 (14.21%)
occurrences (all)	10	19	28
Dyspnoea			
subjects affected / exposed	3 / 196 (1.53%)	3 / 199 (1.51%)	5 / 197 (2.54%)
occurrences (all)	3	3	5
Dyspnoea exertional			
subjects affected / exposed	22 / 196 (11.22%)	22 / 199 (11.06%)	30 / 197 (15.23%)
occurrences (all)	22	22	30
Epistaxis			

subjects affected / exposed	7 / 196 (3.57%)	2 / 199 (1.01%)	12 / 197 (6.09%)
occurrences (all)	7	2	12
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	6 / 196 (3.06%)	9 / 199 (4.52%)	16 / 197 (8.12%)
occurrences (all)	6	9	16
Dry skin			
subjects affected / exposed	15 / 196 (7.65%)	22 / 199 (11.06%)	25 / 197 (12.69%)
occurrences (all)	15	22	25
Pruritus			
subjects affected / exposed	21 / 196 (10.71%)	24 / 199 (12.06%)	22 / 197 (11.17%)
occurrences (all)	22	26	22
Pruritus generalised			
subjects affected / exposed	9 / 196 (4.59%)	16 / 199 (8.04%)	15 / 197 (7.61%)
occurrences (all)	9	17	16
Rash			
subjects affected / exposed	24 / 196 (12.24%)	27 / 199 (13.57%)	39 / 197 (19.80%)
occurrences (all)	25	30	39
Psychiatric disorders			
Anxiety			
subjects affected / exposed	12 / 196 (6.12%)	16 / 199 (8.04%)	17 / 197 (8.63%)
occurrences (all)	12	17	17
Depressed mood			
subjects affected / exposed	8 / 196 (4.08%)	11 / 199 (5.53%)	17 / 197 (8.63%)
occurrences (all)	8	11	17
Depression			
subjects affected / exposed	1 / 196 (0.51%)	8 / 199 (4.02%)	10 / 197 (5.08%)
occurrences (all)	1	8	10
Insomnia			
subjects affected / exposed	47 / 196 (23.98%)	56 / 199 (28.14%)	50 / 197 (25.38%)
occurrences (all)	48	59	51
Irritability			
subjects affected / exposed	17 / 196 (8.67%)	25 / 199 (12.56%)	21 / 197 (10.66%)
occurrences (all)	17	25	21
Mood swings			

subjects affected / exposed	3 / 196 (1.53%)	7 / 199 (3.52%)	5 / 197 (2.54%)
occurrences (all)	3	7	5
Sleep disorder			
subjects affected / exposed	15 / 196 (7.65%)	7 / 199 (3.52%)	11 / 197 (5.58%)
occurrences (all)	15	7	11
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	10 / 196 (5.10%)	15 / 199 (7.54%)	25 / 197 (12.69%)
occurrences (all)	10	17	25
Back pain			
subjects affected / exposed	10 / 196 (5.10%)	14 / 199 (7.04%)	15 / 197 (7.61%)
occurrences (all)	11	14	15
Musculoskeletal pain			
subjects affected / exposed	9 / 196 (4.59%)	22 / 199 (11.06%)	11 / 197 (5.58%)
occurrences (all)	9	27	12
Myalgia			
subjects affected / exposed	12 / 196 (6.12%)	19 / 199 (9.55%)	33 / 197 (16.75%)
occurrences (all)	12	19	34
Neck pain			
subjects affected / exposed	2 / 196 (1.02%)	2 / 199 (1.01%)	1 / 197 (0.51%)
occurrences (all)	2	2	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	12 / 196 (6.12%)	14 / 199 (7.04%)	7 / 197 (3.55%)
occurrences (all)	12	16	7
Upper respiratory tract infection			
subjects affected / exposed	8 / 196 (4.08%)	10 / 199 (5.03%)	3 / 197 (1.52%)
occurrences (all)	8	10	3
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	13 / 196 (6.63%)	16 / 199 (8.04%)	35 / 197 (17.77%)
occurrences (all)	13	16	35

Non-serious adverse events	Retreatment Period: SOF+RBV+Peg- IFN 12 Weeks		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 30 (96.67%)		

Investigations Platelet count decreased subjects affected / exposed occurrences (all)	 2 / 30 (6.67%) 2		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Dizziness postural subjects affected / exposed occurrences (all) Dysgeusia subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Lethargy subjects affected / exposed occurrences (all) Memory impairment subjects affected / exposed occurrences (all)	 2 / 30 (6.67%) 3 0 / 30 (0.00%) 0 1 / 30 (3.33%) 1 12 / 30 (40.00%) 13 1 / 30 (3.33%) 1 1 / 30 (3.33%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all)	 0 / 30 (0.00%) 0 2 / 30 (6.67%) 2		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) Chills	 0 / 30 (0.00%) 0 		

subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
Fatigue subjects affected / exposed occurrences (all)	18 / 30 (60.00%) 18		
Influenza like illness subjects affected / exposed occurrences (all)	6 / 30 (20.00%) 6		
Injection site rash subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2		
Pyrexia subjects affected / exposed occurrences (all)	6 / 30 (20.00%) 8		
Eye disorders Dry eye subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0		
Diarrhoea subjects affected / exposed occurrences (all)	3 / 30 (10.00%) 4		
Dry mouth subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0		
Dyspepsia subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
Gastrooesophageal reflux disease			

subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	3		
Mouth ulceration			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Nausea			
subjects affected / exposed	7 / 30 (23.33%)		
occurrences (all)	7		
Vomiting			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Dyspnoea			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Dyspnoea exertional			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Epistaxis			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Dry skin			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
Pruritus			
subjects affected / exposed	6 / 30 (20.00%)		
occurrences (all)	7		
Pruritus generalised			

subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	6 / 30 (20.00%)		
occurrences (all)	6		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Depressed mood			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Depression			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
Insomnia			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Irritability			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
Mood swings			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
Sleep disorder			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
Back pain			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Musculoskeletal pain			

subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	7 / 30 (23.33%)		
occurrences (all)	7		
Neck pain			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 July 2013	• Corrections were made to the testing included in the optional viral dynamic substudy, as well as to the sample collection at baseline, on-treatment, and early termination visits.
24 October 2013	• The list of clinical laboratory analytes was updated to include additional tests and the stopping requirements for SOF were clarified, based on Food and Drug Administration (FDA) recommendations. • Typographical errors in the study design and inclusion criteria were corrected, and the specimen storage guidelines and disallowed concomitant medication list were updated. In addition, the power size calculations were modified as required to demonstrate superiority across study arms.
01 April 2015	• The results of the primary efficacy endpoint interim analysis (for SVR12) indicated that treatment with SOF+Peg-IFN+RBV for 12 weeks resulted in a higher SVR12 rate compared with SOF+RBV, both for subjects treated for 16 weeks and for subjects treated for 24 weeks. Based on these data and considering that all subjects were required to be considered IFN eligible in the initial study protocol, a retreatment substudy was incorporated in the study design. In the substudy, treatment with SOF+Peg-IFN+RBV was offered to subjects who were randomized to receive SOF+RBV for 16 or 24 weeks and experienced virologic failure during treatment or relapsed at or before posttreatment Week 24.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/26248087