Clinical trial results:
An Open-Label Study of GS-7977 + Ribavirin With or Without Peginterferon Alfa-2a in Subjects With Chronic HCV Infection Who Participated in Prior Gilead HCV Studies

Summary

EudraCT number	2012-000571-16
Trial protocol	AT GB SE EE DE NL ES PL CZ
Global end of trial date	22 December 2014

Results information

Result version number	v1 (current)
This version publication date	13 May 2016
First version publication date	13 May 2016

Trial information

Trial identification

Sponsor protocol code	GS-US-334-0109

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01625338
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 Information Desk, Gilead Sciences International Ltd, +44 1223897 496, clinical.trials@gilead.com
Scientific contact	Clinical Trial Information Desk, Gilead Sciences International Ltd, +44 1223897 496, clinical.trials@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	22 December 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 December 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study will evaluate the efficacy, safety, and tolerability of sofosbuvir (SOF; GS-7977) in combination with ribavirin (RBV) with or
without pegylated interferon (Peg-IFN) in adults with chronic hepatitis C virus (HCV) infection who participated in a prior Gilead HCV
study and have not achieved sustained virologic response (SVR).

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	22 June 2012
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	Netherlands: 10
Country: Number of subjects enrolled	Poland: 9
Country: Number of subjects enrolled	Spain: 11
Country: Number of subjects enrolled	Sweden: 10
Country: Number of subjects enrolled	United Kingdom: 21
Country: Number of subjects enrolled	Austria: 4
Country: Number of subjects enrolled	Czech Republic: 1
Country: Number of subjects enrolled	Estonia: 6
Country: Number of subjects enrolled	France: 23
Country: Number of subjects enrolled	Germany: 33
Country: Number of subjects enrolled	Italy: 14
Country: Number of subjects enrolled	United States: 280
Country: Number of subjects enrolled	New Zealand: 40
Country: Number of subjects enrolled	Canada: 30

Country: Number of subjects enrolled	Australia: 42
Worldwide total number of subjects	534
EEA total number of subjects	142

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)	502
From 65 to 84 years	32
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at a total of 152 study sites from their prior Gilead study in North America, Europe, Australia, and New Zealand. The first participant was screened on 22 June 2012. The last study visit occurred on 22 December 2014.

Pre-assignment

Screening details:

585 participants were screened.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	SOF+RBV 12 Weeks

Arm description:

SOF+RBV for 12 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:

Sofosbuvir (SOF) 400 mg 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:

Ribavirin (RBV) 1000 or 1200 mg daily based on weight

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:

Sofosbuvir (SOF) 400 mg 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:
Ribavirin (RBV) 1000 or 1200 mg daily based on weight

Arm title	SOF+RBV+Peg-IFN 12 Weeks

Arm description:
SOF+RBV+Peg-IFN for 12 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:
Sofosbuvir (SOF) 400 mg 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:
Ribavirin (RBV) 1000 or 1200 mg daily based on weight

Investigational medicinal product name	Pegylated interferon
Investigational medicinal product code	
Other name	PEGASYS®
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:
Pegylated interferon (Peg-IFN) 180 µg once weekly

Number of subjects in period 1[1]	SOF+RBV 12 Weeks	SOF+RBV 24 Weeks	SOF+RBV+Peg-IFN 12 Weeks
Started	114	200	219
Completed	82	156	181
Not completed	32	44	38
Subject Withdrew Consent	1	-	2
Adverse event, non-fatal	1	-	1
Efficacy Failure	27	39	31
Study Discontinued by Sponsor	-	-	1
Investigator Decision	-	2	1
Lost to follow-up	3	3	2

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: One participant who was enrolled but not treated is not included in the subject disposition table.

Baseline characteristics

Reporting groups	
Reporting group title	SOF+RBV 12 Weeks
Reporting group description: SOF+RBV for 12 weeks	
Reporting group title	SOF+RBV 24 Weeks
Reporting group description: SOF+RBV for 24 weeks	
Reporting group title	SOF+RBV+Peg-IFN 12 Weeks
Reporting group description: SOF+RBV+Peg-IFN for 12 weeks	

Reporting group values	SOF+RBV 12 Weeks	SOF+RBV 24 Weeks	SOF+RBV+Peg-IFN 12 Weeks
Number of subjects	114	200	219
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	53	52	53
standard deviation	± 9.6	± 7.6	± 10
Gender categorical Units: Subjects			
Female	54	50	60
Male	60	150	159
Race Units: Subjects			
White	105	184	187
Black Or African American	4	2	20
Asian	2	6	8
Other	1	3	2
Not Permitted	0	2	2
American Indian Or Alaska Native	2	1	0
Native Hawaiian Or Other Pacific Islander	0	2	0
Ethnicity Units: Subjects			
Hispanic or Latino	19	12	20
Not Hispanic or Latino	95	187	197
Not Permitted	0	1	2
HCV Genotype Units: Subjects			
Genotype 1	0	2	134
Genotype 2	62	10	8
Genotype 3	52	180	74
Genotype 4	0	7	3
Indeterminate	0	1	0

Cirrhosis Status Units: Subjects			
No	89	138	183
Yes	25	62	36
IL28b Status			
CC, CT, and TT alleles are different forms of the IL28b gene.			
Units: Subjects			
CC	38	59	47
CT	61	103	127
TT	13	35	40
Missing	2	3	5
HCV RNA Category Units: Subjects			
< 800,000 IU/mL	30	44	36
≥ 800,000 IU/mL	84	156	183
HCV RNA Units: log10 IU/mL			
arithmetic mean	6.3	6.4	6.4
standard deviation	± 0.87	± 0.7	± 0.64

Reporting group values	Total		
Number of subjects	533		
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Female	164		
Male	369		
Race Units: Subjects			
White	476		
Black Or African American	26		
Asian	16		
Other	6		
Not Permitted	4		
American Indian Or Alaska Native	3		
Native Hawaiian Or Other Pacific Islander	2		
Ethnicity Units: Subjects			
Hispanic or Latino	51		
Not Hispanic or Latino	479		
Not Permitted	3		
HCV Genotype Units: Subjects			
Genotype 1	136		

Genotype 2	80		
Genotype 3	306		
Genotype 4	10		
Indeterminate	1		
Cirrhosis Status Units: Subjects			
No	410		
Yes	123		
IL28b Status			
CC, CT, and TT alleles are different forms of the IL28b gene.			
Units: Subjects			
CC	144		
CT	291		
TT	88		
Missing	10		
HCV RNA Category Units: Subjects			
< 800,000 IU/mL	110		
≥ 800,000 IU/mL	423		
HCV RNA Units: log10 IU/mL arithmetic mean standard deviation	- 		

End points

End points reporting groups

Reporting group title	SOF+RBV 12 Weeks
Reporting group description: SOF+RBV for 12 weeks	
Reporting group title	SOF+RBV 24 Weeks
Reporting group description: SOF+RBV for 24 weeks	
Reporting group title	SOF+RBV+Peg-IFN 12 Weeks
Reporting group 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, 25 IU/mL) at 12 weeks after stopping study treatment.

Full Analysis Set: participants who were enrolled 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 12 Weeks	SOF+RBV 24 Weeks	SOF+RBV+Peg-IFN 12 Weeks	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	114	200	219	
Units: percentage of participants				
number (not applicable)	71.9	77.5	82.6	

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 who were enrolled 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 12 Weeks	SOF+RBV 24 Weeks	SOF+RBV+Peg -IFN 12 Weeks	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	114	200	219	
Units: percentage of participants]				
number (not applicable)	0.9	1	3.7	

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

End point type	Secondary

End point timeframe:

Posttreatment Weeks 4 and 24

End point values	SOF+RBV 12 Weeks	SOF+RBV 24 Weeks	SOF+RBV+Peg -IFN 12 Weeks	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	114	200	219	
Units: percentage of participants				
number (not applicable)				
SVR4	73.7	81.5	87.2	
SVR24	71.9	76	82.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With On-treatment Virologic Failure

End point title	Percentage of Participants With 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)

Full Analysis Set

End point type	Secondary

End point timeframe:

Up to 24 weeks

End point values	SOF+RBV 12 Weeks	SOF+RBV 24 Weeks	SOF+RBV+Peg -IFN 12 Weeks	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	114	200	219	
Units: percentage of participants				
number (not applicable)	0.9	0.5	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Viral Relapse

End point title	Percentage of Participants With Viral Relapse

End point description:

Viral relapse was defined as HCV RNA ≥ LLOQ during the posttreatment period having achieved HCV RNA < LLOQ at end of treatment, confirmed with 2 consecutive values or last available posttreatment 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 12 Weeks	SOF+RBV 24 Weeks	SOF+RBV+Peg -IFN 12 Weeks	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	113	199	219	
Units: percentage of participants				
number (not applicable)	25.7	20.6	16.4	

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	
Adverse event reporting additional description: Safety Analysis Set	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1
Reporting groups	
Reporting group title	SOF+RBV 12 Weeks
Reporting group description: SOF+RBV for 12 weeks	
Reporting group title	SOF+RBV 24 Weeks
Reporting group description: SOF+RBV for 24 weeks	
Reporting group title	SOF+RBV+Peg-IFN 12 Weeks
Reporting group description: SOF+RBV+Peg-IFN for 12 weeks	

Serious adverse events	SOF+RBV 12 Weeks	SOF+RBV 24 Weeks	SOF+RBV+Peg-IFN 12 Weeks
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 114 (3.51%)	11 / 200 (5.50%)	4 / 219 (1.83%)
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)			
Hepatocellular carcinoma			
subjects affected / exposed	1 / 114 (0.88%)	1 / 200 (0.50%)	0 / 219 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ligament rupture			
subjects affected / exposed	0 / 114 (0.00%)	1 / 200 (0.50%)	0 / 219 (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
Multiple injuries			

subjects affected / exposed	0 / 114 (0.00%)	1 / 200 (0.50%)	0 / 219 (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
Post procedural haemorrhage			
subjects affected / exposed	1 / 114 (0.88%)	0 / 200 (0.00%)	0 / 219 (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
Road traffic accident			
subjects affected / exposed	0 / 114 (0.00%)	1 / 200 (0.50%)	0 / 219 (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
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 114 (0.00%)	1 / 200 (0.50%)	0 / 219 (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
Presyncope			
subjects affected / exposed	0 / 114 (0.00%)	1 / 200 (0.50%)	0 / 219 (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
Myelitis transverse			
subjects affected / exposed	1 / 114 (0.88%)	0 / 200 (0.00%)	0 / 219 (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
Social circumstances			
Social stay hospitalisation			
subjects affected / exposed	0 / 114 (0.00%)	1 / 200 (0.50%)	0 / 219 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 114 (0.00%)	1 / 200 (0.50%)	0 / 219 (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

Dysphagia			
subjects affected / exposed	0 / 114 (0.00%)	0 / 200 (0.00%)	1 / 219 (0.46%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 114 (0.00%)	1 / 200 (0.50%)	0 / 219 (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
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 114 (0.00%)	1 / 200 (0.50%)	0 / 219 (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
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 114 (0.00%)	0 / 200 (0.00%)	1 / 219 (0.46%)
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			
Suicide attempt			
subjects affected / exposed	1 / 114 (0.88%)	0 / 200 (0.00%)	1 / 219 (0.46%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Affective disorder			
subjects affected / exposed	0 / 114 (0.00%)	1 / 200 (0.50%)	0 / 219 (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
Insomnia			
subjects affected / exposed	0 / 114 (0.00%)	1 / 200 (0.50%)	0 / 219 (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
Mania			

subjects affected / exposed	0 / 114 (0.00%)	1 / 200 (0.50%)	0 / 219 (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
Psychotic disorder			
subjects affected / exposed	0 / 114 (0.00%)	1 / 200 (0.50%)	0 / 219 (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
Substance-induced psychotic disorder			
subjects affected / exposed	0 / 114 (0.00%)	0 / 200 (0.00%)	1 / 219 (0.46%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Rotator cuff syndrome			
subjects affected / exposed	0 / 114 (0.00%)	1 / 200 (0.50%)	0 / 219 (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
Infections and infestations			
Meningitis aseptic			
subjects affected / exposed	0 / 114 (0.00%)	1 / 200 (0.50%)	0 / 219 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	SOF+RBV 12 Weeks	SOF+RBV 24 Weeks	SOF+RBV+Peg-IFN 12 Weeks
Total subjects affected by non-serious adverse events			
subjects affected / exposed	92 / 114 (80.70%)	167 / 200 (83.50%)	194 / 219 (88.58%)
Nervous system disorders			
Headache			
subjects affected / exposed	15 / 114 (13.16%)	57 / 200 (28.50%)	71 / 219 (32.42%)
occurrences (all)	15	64	75
Dizziness			
subjects affected / exposed	4 / 114 (3.51%)	13 / 200 (6.50%)	23 / 219 (10.50%)
occurrences (all)	4	13	25

Dysgeusia			
subjects affected / exposed	3 / 114 (2.63%)	0 / 200 (0.00%)	12 / 219 (5.48%)
occurrences (all)	3	0	12
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	13 / 114 (11.40%)	12 / 200 (6.00%)	26 / 219 (11.87%)
occurrences (all)	13	13	27
Neutropenia			
subjects affected / exposed	0 / 114 (0.00%)	0 / 200 (0.00%)	38 / 219 (17.35%)
occurrences (all)	0	0	40
Leukopenia			
subjects affected / exposed	0 / 114 (0.00%)	0 / 200 (0.00%)	11 / 219 (5.02%)
occurrences (all)	0	0	12
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	33 / 114 (28.95%)	66 / 200 (33.00%)	97 / 219 (44.29%)
occurrences (all)	34	71	99
Influenza like illness			
subjects affected / exposed	6 / 114 (5.26%)	5 / 200 (2.50%)	45 / 219 (20.55%)
occurrences (all)	6	5	52
Asthenia			
subjects affected / exposed	5 / 114 (4.39%)	9 / 200 (4.50%)	19 / 219 (8.68%)
occurrences (all)	5	9	20
Pyrexia			
subjects affected / exposed	5 / 114 (4.39%)	1 / 200 (0.50%)	27 / 219 (12.33%)
occurrences (all)	6	1	36
Chills			
subjects affected / exposed	2 / 114 (1.75%)	3 / 200 (1.50%)	19 / 219 (8.68%)
occurrences (all)	2	3	23
Pain			
subjects affected / exposed	2 / 114 (1.75%)	4 / 200 (2.00%)	17 / 219 (7.76%)
occurrences (all)	2	4	18
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	22 / 114 (19.30%)	27 / 200 (13.50%)	52 / 219 (23.74%)
occurrences (all)	22	29	53

Diarrhoea			
subjects affected / exposed	7 / 114 (6.14%)	14 / 200 (7.00%)	28 / 219 (12.79%)
occurrences (all)	7	14	35
Vomiting			
subjects affected / exposed	7 / 114 (6.14%)	7 / 200 (3.50%)	9 / 219 (4.11%)
occurrences (all)	7	10	14
Abdominal pain			
subjects affected / exposed	6 / 114 (5.26%)	7 / 200 (3.50%)	5 / 219 (2.28%)
occurrences (all)	7	8	5
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	11 / 114 (9.65%)	11 / 200 (5.50%)	33 / 219 (15.07%)
occurrences (all)	11	11	33
Dyspnoea			
subjects affected / exposed	6 / 114 (5.26%)	12 / 200 (6.00%)	11 / 219 (5.02%)
occurrences (all)	6	14	11
Dyspnoea exertional			
subjects affected / exposed	5 / 114 (4.39%)	7 / 200 (3.50%)	13 / 219 (5.94%)
occurrences (all)	5	7	13
Oropharyngeal pain			
subjects affected / exposed	3 / 114 (2.63%)	4 / 200 (2.00%)	12 / 219 (5.48%)
occurrences (all)	3	4	12
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	15 / 114 (13.16%)	23 / 200 (11.50%)	40 / 219 (18.26%)
occurrences (all)	15	24	40
Rash			
subjects affected / exposed	13 / 114 (11.40%)	19 / 200 (9.50%)	35 / 219 (15.98%)
occurrences (all)	14	19	36
Dry skin			
subjects affected / exposed	6 / 114 (5.26%)	14 / 200 (7.00%)	17 / 219 (7.76%)
occurrences (all)	7	14	17
Psychiatric disorders			
Insomnia			
subjects affected / exposed	18 / 114 (15.79%)	34 / 200 (17.00%)	37 / 219 (16.89%)
occurrences (all)	18	36	38

Irritability			
subjects affected / exposed	5 / 114 (4.39%)	27 / 200 (13.50%)	38 / 219 (17.35%)
occurrences (all)	5	28	38
Depression			
subjects affected / exposed	7 / 114 (6.14%)	21 / 200 (10.50%)	14 / 219 (6.39%)
occurrences (all)	7	22	14
Anxiety			
subjects affected / exposed	6 / 114 (5.26%)	11 / 200 (5.50%)	14 / 219 (6.39%)
occurrences (all)	6	11	14
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	13 / 114 (11.40%)	21 / 200 (10.50%)	37 / 219 (16.89%)
occurrences (all)	13	24	40
Myalgia			
subjects affected / exposed	8 / 114 (7.02%)	9 / 200 (4.50%)	45 / 219 (20.55%)
occurrences (all)	8	10	47
Muscle spasms			
subjects affected / exposed	7 / 114 (6.14%)	17 / 200 (8.50%)	11 / 219 (5.02%)
occurrences (all)	9	18	11
Back pain			
subjects affected / exposed	9 / 114 (7.89%)	11 / 200 (5.50%)	13 / 219 (5.94%)
occurrences (all)	10	11	15
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	9 / 114 (7.89%)	22 / 200 (11.00%)	4 / 219 (1.83%)
occurrences (all)	10	25	5
Upper respiratory tract infection			
subjects affected / exposed	7 / 114 (6.14%)	9 / 200 (4.50%)	2 / 219 (0.91%)
occurrences (all)	7	9	2
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 114 (2.63%)	8 / 200 (4.00%)	32 / 219 (14.61%)
occurrences (all)	3	8	34

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 February 2013	Incorporated 2 additional treatment groups: (1) SOF+RBV for a duration of 24 weeks for subjects with genotype 2 or 3 HCV infection and (2) SOF+Peg-IFN+RBV for a duration of 12 weeks for subjects with any genotype of HCV infection.
10 May 2013	Provided rationale and guidance for genotype for each treatment group, updated exclusion criteria to be in agreement with Peg-IFN contraindications, and added guidelines for toxicity management of Peg-IFN.

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: