Clinical trial results:
A Phase 3, Multicenter, Randomized, Double-Blind, Placebo Controlled Study to Investigate the Efficacy and Safety of GS-7977 + Ribavirin for 12 Weeks in Treatment Naïve and Treatment Experienced Subjects with Chronic Genotype 2 or 3 HCV Infection

Summary

EudraCT number	2012-001942-16
Trial protocol	EE AT NL DE GB SE ES PL
Global end of trial date	08 January 2014

Results information

Result version number	v1 (current)
This version publication date	22 March 2016
First version publication date	05 August 2015

Trial information

Trial identification

Sponsor protocol code	GS-US-334-0133

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01682720
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	08 January 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 January 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study evaluated the safety, tolerability, and antiviral efficacy of sofosbuvir (SOF; GS-7977) with ribavirin (RBV) in participants with genotype 2 or 3 hepatitis C virus (HCV) infection.

Protection of trial subjects:

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

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 September 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: 25
Country: Number of subjects enrolled	Poland: 22
Country: Number of subjects enrolled	Spain: 48
Country: Number of subjects enrolled	Sweden: 24
Country: Number of subjects enrolled	United Kingdom: 55
Country: Number of subjects enrolled	Austria: 18
Country: Number of subjects enrolled	Estonia: 15
Country: Number of subjects enrolled	Germany: 69
Country: Number of subjects enrolled	Italy: 62
Country: Number of subjects enrolled	France: 81
Worldwide total number of subjects	419
EEA total number of subjects	419

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)	386
From 65 to 84 years	33
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at a total of 77 study sites in Europe. The first participant was screened on 19 September 2012. The last participant observation occurred on 08 January 2014.

Pre-assignment

Screening details:

475 participants were screened and 421 were randomized.
419 participants were randomized and received at least 1 dose of study drug (Safety Analysis Set).
344 participants with genotype 2 or 3 HCV infection were randomized and received at least 1 dose of sofosbuvir (Full Analysis Set).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo 12 Weeks (GT2/3)

Arm description:

Placebo to match sofosbuvir (SOF) + placebo to match ribavirin (RBV) for 12 weeks in participants with genotype (GT) 2 or 3 HCV infection

Arm type	Placebo
Investigational medicinal product name	SOF Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo to match SOF administered orally once daily

Investigational medicinal product name	RBV Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo to match RBV administered orally in a divided daily dose

Arm title	SOF + RBV 12 Weeks (GT2)

Arm description:

SOF + RBV for 12 weeks in participants with genotype 2 HCV infection

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

Dosage and administration details:

SOF 400 mg tablet administered orally once daily

Investigational medicinal product name	RBV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

RBV 200 mg tablets administered orally 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 12 Weeks (GT3)

Arm description:

SOF + RBV for 12 weeks in participants with genotype 3 HCV infection

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

Dosage and administration details:

SOF 400 mg tablet administered orally once daily

Investigational medicinal product name	RBV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

RBV 200 mg tablets administered orally 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 (GT3)

Arm description:

SOF + RBV for 24 weeks in participants with genotype 3 HCV infection

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

Dosage and administration details:

SOF 400 mg tablet administered orally once daily

Investigational medicinal product name	RBV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

RBV 200 mg tablets administered orally in a divided daily dose according to package insert weight-based dosing recommendations (< 75 kg = 1000 mg and ≥ 75 kg = 1200 mg)

Number of subjects in period 1	Placebo 12 Weeks (GT2/3)	SOF + RBV 12 Weeks (GT2)	SOF + RBV 12 Weeks (GT3)
Started	85	73	11
Completed	0	69	5
Not completed	85	4	6
Efficacy failure	-	3	3
Consent withdrawn by subject	-	-	2
Adverse event, non-fatal	1	-	1
Terminated by sponsor	83	-	-
Lost to follow-up	1	1	-
Efficacy faiure	-	-	-

Number of subjects in period 1	SOF + RBV 24 Weeks (GT3)
Started	250
Completed	211
Not completed	39
Efficacy failure	-
Consent withdrawn by subject	2
Adverse event, non-fatal	1
Terminated by sponsor	-
Lost to follow-up	6
Efficacy faiure	30

Baseline characteristics

Reporting groups	
Reporting group title	Placebo 12 Weeks (GT2/3)
Reporting group description:	
Placebo to match sofosbuvir (SOF) + placebo to match ribavirin (RBV) for 12 weeks in participants with genotype (GT) 2 or 3 HCV infection	
Reporting group title	SOF + RBV 12 Weeks (GT2)
Reporting group description:	
SOF + RBV for 12 weeks in participants with genotype 2 HCV infection	
Reporting group title	SOF + RBV 12 Weeks (GT3)
Reporting group description:	
SOF + RBV for 12 weeks in participants with genotype 3 HCV infection	
Reporting group title	SOF + RBV 24 Weeks (GT3)
Reporting group description:	
SOF + RBV for 24 weeks in participants with genotype 3 HCV infection	

Reporting group values	Placebo 12 Weeks (GT2/3)	SOF + RBV 12 Weeks (GT2)	SOF + RBV 12 Weeks (GT3)
Number of subjects	85	73	11
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	49	58	46
standard deviation	± 10.5	± 10.1	± 8.8
Gender categorical Units: Subjects			
Female	36	33	5
Male	49	40	6
HCV Genotype Units: Subjects			
Genotype 2	18	73	0
Genotype 3	67	0	11
Liver cirrhosis Units: Subjects			
No	68	62	9
Yes	17	11	2
HCV RNA category Units: Subjects			
< 6 log10 IU/mL	21	16	4
≥ 6 log10 IU/mL	64	57	7
Prior HCV treatment experience Units: Subjects			
Experienced	50	41	9
Naive	35	32	2
Response to prior HCV treatment Units: Subjects			

Interferon intolerant	0	3	0
Nonresponse	18	10	4
Relapse/breakthrough	32	28	5
N/A (treatment-naive)	35	32	2
Interferon eligibility Units: Subjects			
Interferon eligible	30	27	2
Interferon ineligible	5	5	0
N/A (treatment-experienced)	50	41	9
Race Units: Subjects			
Black or African American	1	5	0
White	81	65	11
Asian	3	1	0
Not permitted	0	2	0
Ethnicity Units: Subjects			
Hispanic or Latino	10	6	1
Not Hispanic or Latino	71	65	10
Not permitted	4	2	0
HCV RNA Units: log10 IU/mL			
arithmetic mean	6.5	6.5	6.2
standard deviation	± 0.69	± 0.7	± 0.77

Reporting group values	SOF + RBV 24 Weeks (GT3)	Total	
Number of subjects	250	419	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	48		
standard deviation	± 10.1	-	
Gender categorical Units: Subjects			
Female	95	169	
Male	155	250	
HCV Genotype Units: Subjects			
Genotype 2	0	91	
Genotype 3	250	328	
Liver cirrhosis Units: Subjects			
No	190	329	
Yes	60	90	
HCV RNA category Units: Subjects			
< 6 log10 IU/mL	72	113	
≥ 6 log10 IU/mL	178	306	
Prior HCV treatment experience			

Units: Subjects			
Experienced	145	245	
Naive	105	174	
Response to prior HCV treatment Units: Subjects			
Interferon intolerant	10	13	
Nonresponse	41	73	
Relapse/breakthrough	94	159	
N/A (treatment-naive)	105	174	
Interferon eligibility Units: Subjects			
Interferon eligible	94	153	
Interferon ineligible	11	21	
N/A (treatment-experienced)	145	245	
Race Units: Subjects			
Black or African American	0	6	
White	236	393	
Asian	9	13	
Not permitted	5	7	
Ethnicity Units: Subjects			
Hispanic or Latino	36	53	
Not Hispanic or Latino	203	349	
Not permitted	11	17	
HCV RNA Units: log10 IU/mL			
arithmetic mean	6.3		
standard deviation	± 0.74	-	

End points

End points reporting groups

Reporting group title	Placebo 12 Weeks (GT2/3)
Reporting group description:	
Placebo to match sofosbuvir (SOF) + placebo to match ribavirin (RBV) for 12 weeks in participants with genotype (GT) 2 or 3 HCV infection	
Reporting group title	SOF + RBV 12 Weeks (GT2)
Reporting group description:	
SOF + RBV for 12 weeks in participants with genotype 2 HCV infection	
Reporting group title	SOF + RBV 12 Weeks (GT3)
Reporting group description:	
SOF + RBV for 12 weeks in participants with genotype 3 HCV infection	
Reporting group title	SOF + RBV 24 Weeks (GT3)
Reporting group description:	
SOF + RBV for 24 weeks in participants with genotype 3 HCV infection	
Subject analysis set title	SOF + RBV 12 Weeks (GT2/3)
Subject analysis set type	Safety analysis
Subject analysis set description:	
SOF + RBV for 12 weeks in participants with genotype 2 or 3 HCV infection	

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

End point title	Percentage of Participants With Sustained Virologic Response 12 Weeks After Discontinuation of Therapy (SVR12)[1][2]
End point description:	
SVR12 was defined as HCV RNA < the lower limit of quantitation (LLOQ, ie, < 25 IU/mL) 12 weeks following the last dose of study drug. SVR data was not collected for the Placebo 12 Weeks (GT2/3) group. Full Analysis Set: participants with genotype 2 or 3 HCV infection were randomized and received at least 1 dose of SOF.	
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 intergroup comparison was performed because the GT2 12 week and GT3 24 week groups were distinct in demographics and treatment.
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Consistent with the termination of study by sponsor provided for in Protocol Amendment 2, and because participants in the placebo group did not receive active treatment, no data for sustained virologic response was collected for the Placebo 12 Weeks (GT2/3) group.

End point values	SOF + RBV 12 Weeks (GT2)	SOF + RBV 12 Weeks (GT3)	SOF + RBV 24 Weeks (GT3)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	11	250	
Units: percentage of participants				
number (not applicable)	93.2	27.3	85.2	

Statistical analyses

No statistical analyses for this end point

Primary: Adverse Events Leading to Permanent Discontinuation of Study Drug(s)

End point title	Adverse Events Leading to Permanent Discontinuation of Study Drug(s)[3][4]

End point description:

The percentage of participants experiencing an adverse event leading to permanent discontinuation of study drug(s) was analyzed.
Safety Analysis Set: participants who were randomized 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 intergroup comparison was performed because the various groups were distinct in demographics and treatment.
[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Adverse events for the SOF 12 Weeks (GT2) SOF 12 Weeks (GT3) groups were collected and are reported as the SOF 12 Weeks (GT2/3) group.

End point values	Placebo 12 Weeks (GT2/3)	SOF + RBV 24 Weeks (GT3)	SOF + RBV 12 Weeks (GT2/3)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	85	250	84	
Units: percentage of participants				
number (not applicable)	1.2	0.4	1.2	

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Participants With Sustained Virologic Response at 4 and 24 Weeks After Discontinuation of Therapy (SVR4 and SVR24)[5]

End point description:

SVR4 and SVR24 was defined as HCV RNA < LLOQ at 4 and 24 weeks following the last dose of study drug, respectively. SVR data was not collected for the Placebo 12 Weeks (GT2/3) group.
Full Analysis Set

End point type	Secondary

End point timeframe:

Posttreatment Weeks 4 and 24

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Consistent with the termination of study by sponsor provided for in Protocol Amendment 2, and because participants in the placebo group did not receive active treatment, no data for sustained virologic response was collected for the Placebo 12 Weeks (GT2/3) group.

End point values	SOF + RBV 12 Weeks (GT2)	SOF + RBV 12 Weeks (GT3)	SOF + RBV 24 Weeks (GT3)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	11	250	
Units: percentage of participants				
number (not applicable)				
SVR4	93.2	45.5	87.2	
SVR24	93.2	27.3	84.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing Viral Breakthrough or Viral Relapse

End point title	Percentage of Participants Experiencing Viral Breakthrough or Viral Relapse[6]

End point description:

Viral breakthrough was defined as having confirmed detectable HCV RNA levels (HCV RNA > LLOQ) after having previously had undetectable HCV RNA levels (HCV RNA < LLOQ) while on treatment.

Viral relapse was defined as having achieved undetectable HCV RNA levels (HCV RNA < LLOQ) at end of treatment, but did not achieve an SVR.

Data was not collected for the Placebo 12 Weeks (GT2/3) group.

Full Analysis Set

End point type	Secondary

End point timeframe:

Up to Posttreatment Week 24

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Consistent with the termination of study by sponsor provided for in Protocol Amendment 2, and because participants in the placebo group did not receive active treatment, no data for viral breakthrough or viral relapse was collected for the Placebo 12 Weeks (GT2/3) group.

End point values	SOF + RBV 12 Weeks (GT2)	SOF + RBV 12 Weeks (GT3)	SOF + RBV 24 Weeks (GT3)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	11	250	
Units: percentage of participants				
number (not applicable)				
Viral breakthrough	0	0	0.4	
Viral relapse	6.8	54.5	14	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to Week 24 plus 30 days

Adverse event reporting additional description:

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

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Placebo 12 Weeks (GT2/3)

Reporting group description:

Placebo to match SOF + placebo to match RBV for 12 weeks in participants with genotype 2 or 3 HCV infection

Reporting group title	SOF + RBV 12 Weeks (GT2/3)

Reporting group description:

SOF + RBV for 12 weeks in participants with genotype 2 or 3 HCV infection

Reporting group title	SOF + RBV 24 Weeks (GT3)

Reporting group description:

SOF + RBV for 24 weeks in participants with genotype 3 HCV infection

Serious adverse events	Placebo 12 Weeks (GT2/3)	SOF + RBV 12 Weeks (GT2/3)	SOF + RBV 24 Weeks (GT3)
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 85 (2.35%)	0 / 84 (0.00%)	10 / 250 (4.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Amylase increased			
subjects affected / exposed	0 / 85 (0.00%)	0 / 84 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	0 / 85 (0.00%)	0 / 84 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatocellular carcinoma			

subjects affected / exposed	0 / 85 (0.00%)	0 / 84 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 85 (0.00%)	0 / 84 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	0 / 85 (0.00%)	0 / 84 (0.00%)	1 / 250 (0.40%)
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			
Arrhythmia			
subjects affected / exposed	0 / 85 (0.00%)	0 / 84 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Complex regional pain syndrome			
subjects affected / exposed	0 / 85 (0.00%)	0 / 84 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	0 / 250 (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
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 85 (0.00%)	0 / 84 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biliary colic			

subjects affected / exposed	0 / 85 (0.00%)	0 / 84 (0.00%)	1 / 250 (0.40%)
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	0 / 85 (0.00%)	0 / 84 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	0 / 250 (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
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 85 (0.00%)	0 / 84 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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	Placebo 12 Weeks (GT2/3)	SOF + RBV 12 Weeks (GT2/3)	SOF + RBV 24 Weeks (GT3)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	54 / 85 (63.53%)	69 / 84 (82.14%)	212 / 250 (84.80%)
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	2 / 85 (2.35%)	1 / 84 (1.19%)	15 / 250 (6.00%)
occurrences (all)	2	1	15
Dizziness			
subjects affected / exposed	2 / 85 (2.35%)	5 / 84 (5.95%)	19 / 250 (7.60%)
occurrences (all)	2	5	20
Headache			
subjects affected / exposed	23 / 85 (27.06%)	24 / 84 (28.57%)	74 / 250 (29.60%)
occurrences (all)	25	29	101
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	1 / 85 (1.18%)	6 / 84 (7.14%)	17 / 250 (6.80%)
occurrences (all)	1	6	18
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 85 (4.71%)	21 / 84 (25.00%)	53 / 250 (21.20%)
occurrences (all)	4	24	60
Chest pain			
subjects affected / exposed	0 / 85 (0.00%)	5 / 84 (5.95%)	5 / 250 (2.00%)
occurrences (all)	0	5	5
Fatigue			
subjects affected / exposed	16 / 85 (18.82%)	19 / 84 (22.62%)	75 / 250 (30.00%)
occurrences (all)	18	19	78
Influenza like illness			
subjects affected / exposed	5 / 85 (5.88%)	1 / 84 (1.19%)	16 / 250 (6.40%)
occurrences (all)	6	1	17
Irritability			
subjects affected / exposed	3 / 85 (3.53%)	4 / 84 (4.76%)	26 / 250 (10.40%)
occurrences (all)	3	4	28
Pyrexia			
subjects affected / exposed	2 / 85 (2.35%)	7 / 84 (8.33%)	9 / 250 (3.60%)
occurrences (all)	2	9	9
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 85 (4.71%)	1 / 84 (1.19%)	21 / 250 (8.40%)
occurrences (all)	5	1	23
Abdominal pain upper			
subjects affected / exposed	6 / 85 (7.06%)	7 / 84 (8.33%)	15 / 250 (6.00%)
occurrences (all)	6	10	16
Constipation			
subjects affected / exposed	1 / 85 (1.18%)	2 / 84 (2.38%)	13 / 250 (5.20%)
occurrences (all)	1	4	17
Diarrhoea			
subjects affected / exposed	4 / 85 (4.71%)	4 / 84 (4.76%)	30 / 250 (12.00%)
occurrences (all)	4	4	33
Dyspepsia			

subjects affected / exposed	0 / 85 (0.00%)	3 / 84 (3.57%)	15 / 250 (6.00%)
occurrences (all)	0	4	21
Nausea			
subjects affected / exposed	9 / 85 (10.59%)	26 / 84 (30.95%)	33 / 250 (13.20%)
occurrences (all)	9	27	38
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 85 (4.71%)	8 / 84 (9.52%)	27 / 250 (10.80%)
occurrences (all)	4	8	29
Dyspnoea			
subjects affected / exposed	1 / 85 (1.18%)	12 / 84 (14.29%)	27 / 250 (10.80%)
occurrences (all)	1	12	29
Dyspnoea exertional			
subjects affected / exposed	0 / 85 (0.00%)	6 / 84 (7.14%)	9 / 250 (3.60%)
occurrences (all)	0	6	9
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	5 / 85 (5.88%)	8 / 84 (9.52%)	31 / 250 (12.40%)
occurrences (all)	5	8	34
Eczema			
subjects affected / exposed	0 / 85 (0.00%)	3 / 84 (3.57%)	14 / 250 (5.60%)
occurrences (all)	0	3	15
Pruritus			
subjects affected / exposed	8 / 85 (9.41%)	20 / 84 (23.81%)	67 / 250 (26.80%)
occurrences (all)	8	23	74
Rash			
subjects affected / exposed	2 / 85 (2.35%)	1 / 84 (1.19%)	24 / 250 (9.60%)
occurrences (all)	2	1	25
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 85 (2.35%)	1 / 84 (1.19%)	13 / 250 (5.20%)
occurrences (all)	2	1	15
Depressed mood			
subjects affected / exposed	2 / 85 (2.35%)	1 / 84 (1.19%)	13 / 250 (5.20%)
occurrences (all)	2	1	13
Insomnia			

subjects affected / exposed	2 / 85 (2.35%)	9 / 84 (10.71%)	41 / 250 (16.40%)
occurrences (all)	2	9	45
Sleep disorder			
subjects affected / exposed	4 / 85 (4.71%)	4 / 84 (4.76%)	23 / 250 (9.20%)
occurrences (all)	4	4	24
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 85 (7.06%)	3 / 84 (3.57%)	25 / 250 (10.00%)
occurrences (all)	6	3	28
Back pain			
subjects affected / exposed	5 / 85 (5.88%)	5 / 84 (5.95%)	15 / 250 (6.00%)
occurrences (all)	5	5	17
Myalgia			
subjects affected / exposed	1 / 85 (1.18%)	4 / 84 (4.76%)	22 / 250 (8.80%)
occurrences (all)	1	5	22
Pain in extremity			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	13 / 250 (5.20%)
occurrences (all)	1	0	15
Infections and infestations			
Influenza			
subjects affected / exposed	0 / 85 (0.00%)	6 / 84 (7.14%)	12 / 250 (4.80%)
occurrences (all)	0	6	12
Nasopharyngitis			
subjects affected / exposed	9 / 85 (10.59%)	4 / 84 (4.76%)	36 / 250 (14.40%)
occurrences (all)	9	4	41
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 85 (4.71%)	5 / 84 (5.95%)	16 / 250 (6.40%)
occurrences (all)	4	6	16

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 July 2012	Addressed comments received from the Voluntary Harmonisation Procedure (VHP).
06 February 2013	Provided extended treatment duration (to 24 weeks) for participants with genotype 3 HCV infection and for early termination of treatment for placebo recipients.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

There were no limitations affecting the analysis or results.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/24795201