Clinical trial results:
A Phase 2b, Randomized, Double-Blind, Placebo-Controlled Trial Evaluating 16 and 24 Weeks of a Four-Drug Regimen and 24 Weeks of a Three-Drug Regimen of GS-9451, Peginterferon Alfa 2a (PEG, Pegasys®) and Ribavirin (RBV, Copegus®) With and Without Tegobuvir (GS-9190) Followed by Response Guided PEG and RBV in Treatment Naïve Subjects with Chronic Genotype 1 Hepatitis C Virus Infection (Protocol GS-US-196-0140)

Summary

EudraCT number	2010-023952-10
Trial protocol	DE BE GB AT
Global end of trial date	17 September 2013

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-196-0140

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01271790
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	17 September 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 September 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the antiviral efficacy (sustained virologic response [SVR]; defined as undetectable HCV RNA 24 weeks following treatment cessation) of a 3-drug regimen of GS-9451 with peginterferon alfa 2a (PEG) and ribavirin (RBV) followed by response guided PEG/RBV versus a control arm of PEG/RBV therapy for 48 weeks.

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	10 December 2010
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	Poland: 25
Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	United States: 201
Worldwide total number of subjects	239
EEA total number of subjects	38

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)	235
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Europe and North America. The first participant was screened on 10 December 2010. The last study visit occurred on 17 September 2013.

Pre-assignment

Screening details:

239 participants were screened.

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, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	VDV+TGV+Peg-IFN+RBV

Arm description:

VDV+TGV+Peg-IFN+RBV for 16 or 24 weeks; PEG+RBV may have been continued for up to 48 weeks total duration depending on individual response to therapy.

Arm type	Experimental
Investigational medicinal product name	Vedroprevir
Investigational medicinal product code	
Other name	VDV, GS-9451
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Vedroprevir (VDV) 200 mg (2 × 100 mg tablets) administered orally once daily

Investigational medicinal product name	Tegobuvir
Investigational medicinal product code	
Other name	TGV, GS-9190
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Tegobuvir (TGV) 30 mg tablet administered orally twice daily

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

Dosage and administration details:

Peg-IFN 180 µg administered subcutaneously once weekly

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	RBV, Copegus®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ribavirin (RBV) 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	VDV+Peg-IFN+RBV

Arm description:

VDV+placebo to match TGV+Peg-IFN+RBV for 24 weeks; PEG+RBV may have been continued for up to 48 weeks total duration depending on individual response to therapy.

Arm type	Experimental
Investigational medicinal product name	Vedroprevir
Investigational medicinal product code	
Other name	VDV, GS-9451
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Vedroprevir (VDV) 200 mg (2 × 100 mg tablets) administered orally once daily

Investigational medicinal product name	Tegobuvir placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo to match TGV administered orally twice daily

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

Dosage and administration details:

Peg-IFN 180 µg administered subcutaneously once weekly

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	RBV, Copegus®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ribavirin (RBV) 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	Peg-IFN+RBV

Arm description:

Placebo to match VDV+placebo to match TGV+PEG+RBV for 24 weeks; PEG+RBV may have been continued for up to 48 weeks total duration.

Arm type	Experimental
Investigational medicinal product name	Vedroprevir placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo to match VDV administered orally once daily

Investigational medicinal product name	Tegobuvir placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo to match TGV administered orally twice daily

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

Dosage and administration details:

Peg-IFN 180 µg administered subcutaneously once weekly

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	RBV, Copegus®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ribavirin (RBV) 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	VDV+TGV+Peg-IFN+RBV	VDV+Peg-IFN+RBV	Peg-IFN+RBV
Started	119	59	61
Completed	72	32	31
Not completed	47	27	30
Efficacy failure	25	12	13
Participant withdrew consent	8	6	4
Adverse event, non-fatal	4	4	5
Protocol violation	-	-	1
Death	-	-	1
Lost to follow-up	9	4	5
Investigator's discretion	1	1	-
Study discontinued by sponsor	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	VDV+TGV+Peg-IFN+RBV
Reporting group description:	
VDV+TGV+Peg-IFN+RBV for 16 or 24 weeks; PEG+RBV may have been continued for up to 48 weeks total duration depending on individual response to therapy.	
Reporting group title	VDV+Peg-IFN+RBV
Reporting group description:	
VDV+placebo to match TGV+Peg-IFN+RBV for 24 weeks; PEG+RBV may have been continued for up to 48 weeks total duration depending on individual response to therapy.	
Reporting group title	Peg-IFN+RBV
Reporting group description:	
Placebo to match VDV+placebo to match TGV+PEG+RBV for 24 weeks; PEG+RBV may have been continued for up to 48 weeks total duration.	

Reporting group values	VDV+TGV+Peg-IFN+RBV	VDV+Peg-IFN+RBV	Peg-IFN+RBV
Number of subjects	119	59	61
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	47	48	46
standard deviation	± 11.6	± 11.2	± 12.3
Gender categorical Units: Subjects			
Female	44	28	23
Male	75	31	38
Race Units: Subjects			
White	104	46	46
Black or African Heritage	14	9	9
Asian	1	2	4
American Indian or Alaska Native	0	1	0
Other	0	0	2
Not Permitted	0	1	0
Ethnicity Units: Subjects			
Hispanic/Latino	8	3	4
Non-Hispanic/Latino	110	56	56
Not Permitted	1	0	1
HCV RNA Category Units: Subjects			
≤ 800,000 IU/mL	20	11	11
> 800,000 IU/mL	99	48	50
HCV Genotype Units: Subjects			
Genotype 1a	81	39	45

Genotype 1b	38	20	16
IL28b status			
CC and non-CC alleles are different forms of the IL28b gene.			
Units: Subjects			
CC	34	18	20
non-CC	85	41	41
HCV RNA			
Units: log10 IU/mL			
arithmetic mean	6.46	6.55	6.54
standard deviation	± 0.752	± 0.559	± 0.65

Reporting group values	Total		
Number of subjects	239		
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	95		
Male	144		
Race			
Units: Subjects			
White	196		
Black or African Heritage	32		
Asian	7		
American Indian or Alaska Native	1		
Other	2		
Not Permitted	1		
Ethnicity			
Units: Subjects			
Hispanic/Latino	15		
Non-Hispanic/Latino	222		
Not Permitted	2		
HCV RNA Category			
Units: Subjects			
≤ 800,000 IU/mL	42		
> 800,000 IU/mL	197		
HCV Genotype			
Units: Subjects			
Genotype 1a	165		
Genotype 1b	74		
IL28b status			
CC and non-CC alleles are different forms of the IL28b gene.			
Units: Subjects			
CC	72		
non-CC	167		

HCV RNA Units: log10 IU/mL arithmetic mean standard deviation	- 		

End points

End points reporting groups

Reporting group title	VDV+TGV+Peg-IFN+RBV
Reporting group description:	
VDV+TGV+Peg-IFN+RBV for 16 or 24 weeks; PEG+RBV may have been continued for up to 48 weeks total duration depending on individual response to therapy.	
Reporting group title	VDV+Peg-IFN+RBV
Reporting group description:	
VDV+placebo to match TGV+Peg-IFN+RBV for 24 weeks; PEG+RBV may have been continued for up to 48 weeks total duration depending on individual response to therapy.	
Reporting group title	Peg-IFN+RBV
Reporting group description:	
Placebo to match VDV+placebo to match TGV+PEG+RBV for 24 weeks; PEG+RBV may have been continued for up to 48 weeks total duration.	

Primary: Percentage of Participants With Sustained Virologic Response 24 Weeks After Discontinuation of Therapy (SVR24)

End point title	Percentage of Participants With Sustained Virologic Response 24 Weeks After Discontinuation of Therapy (SVR24)
End point description:	
SVR was defined as HCV RNA < 10 IU/mL 24 weeks following the last dose of study drug.	
End point type	Primary
End point timeframe:	
Postttreatment Week 24	

End point values	VDV+TGV+Peg-IFN+RBV	VDV+Peg-IFN+RBV	Peg-IFN+RBV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	119	59	61	
Units: Percentage of participants				
number (not applicable)	64.7	55.9	44.3	

Statistical analyses

Statistical analysis title	Difference in percentage
Comparison groups	Peg-IFN+RBV v VDV+Peg-IFN+RBV
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.168 [2]
Method	Cochran-Mantel-Haenszel

Notes:

[1] - A total sample size of 160 subjects (80 per arm) in Arms 2 and 3 would have approximately 80% power to evaluate superiority of the VDV+Peg-IFN+RBV arm over the Peg-IFN+RBV arm.

[2] - The p-value comparing achievement of SVR is based on the Cochran-Mantel-Haenszel test for stratified proportions.

Secondary: Percentage of Participants With Very Rapid Virologic Response (vRVR)

End point title	Percentage of Participants With Very Rapid Virologic Response (vRVR)

End point description:

vRVR was defined as HCV RNA < 25 IU/mL at Week 2 and Week 4 and HCV RNA < 10 IU/mL at Week 8 maintained through Week 16.

End point type	Secondary

End point timeframe:

Baseline to Week 16

End point values	VDV+TGV+Peg-IFN+RBV	VDV+Peg-IFN+RBV	Peg-IFN+RBV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	119	59	61	
Units: Percentage of participants				
number (not applicable)	56.3	33.9	6.6	

Statistical analyses

Statistical analysis title	Difference in percentage
Comparison groups	VDV+Peg-IFN+RBV v Peg-IFN+RBV
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	< 0.001 [4]
Method	Cochran-Mantel-Haenszel

Notes:

[3] - Comparative analysis

[4] - The p-value is based on the Cochran-Mantel-Haenszel test for stratified proportions.

Secondary: Percentage of Participants With Extended Rapid Virologic Response (eRVR)

End point title	Percentage of Participants With Extended Rapid Virologic Response (eRVR)

End point description:

eRVR was defined as HCV RNA < 25 IU/mL at Week 4 and HCV RNA < 10 IU/mL at Week 8 maintained through Week 24.

End point type	Secondary

End point timeframe:

Baseline to Week 24

End point values	VDV+TGV+Peg-IFN+RBV	VDV+Peg-IFN+RBV	Peg-IFN+RBV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	119	59	61	
Units: Percentage of participants				
number (not applicable)	69.7	61	23	

Statistical analyses

Statistical analysis title	Difference in percentage
Comparison groups	Peg-IFN+RBV v VDV+Peg-IFN+RBV
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	< 0.001 [6]
Method	Cochran-Mantel-Haenszel

Notes:

[5] - Comparative analysis

[6] - The p-value is based on the Cochran-Mantel-Haenszel test for stratified proportions.

Secondary: Percentage of Participants With Partial Early Virologic Response (pEVR)

End point title	Percentage of Participants With Partial Early Virologic Response (pEVR)
End point description: pEVR was defined as at least a 2 log10 IU/mL reduction from baseline in HCV RNA at Week 12.	
End point type	Secondary
End point timeframe: Baseline to Week 12	

End point values	VDV+TGV+Peg-IFN+RBV	VDV+Peg-IFN+RBV	Peg-IFN+RBV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	119	59	61	
Units: Percentage of participants				
number (not applicable)	91.6	88.1	80.3	

Statistical analyses

Statistical analysis title	Difference in percentage
Comparison groups	VDV+Peg-IFN+RBV v Peg-IFN+RBV

Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	other[7]
P-value	= 0.215 [8]
Method	Cochran-Mantel-Haenszel

Notes:

[7] - Comparative analysis

[8] - The p-value is based on the Cochran-Mantel-Haenszel test for stratified proportions.

Secondary: Percentage of participants with Virologic Breakthrough and Relapse

End point title	Percentage of participants with Virologic Breakthrough and Relapse

End point description:

Breakthrough was defined as 2 consecutive values that were undetectable followed (at a later point in time) by 2 consecutive detectable HCV RNA values while on treatment. Relapse was defined as undetectable HCV RNA at end of treatment followed by two consecutive detectable HCV RNA values during off-treatment follow-up.

End point type	Secondary

End point timeframe:

Up to 48 weeks

End point values	VDV+TGV+Peg-IFN+RBV	VDV+Peg-IFN+RBV	Peg-IFN+RBV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	119	59	61	
Units: Percentage of participants				
number (not applicable)				
Breakthrough	4.2	1.7	1.6	
Relapse	12.6	20.3	9.8	

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	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	TGV+VDV+Peg-IFN+RBV
Reporting group description:	
TGV+VDV+Peg-IFN+RBV for 16 or 24 weeks followed by response-guided therapy with Peg-IFN+RBV	
Reporting group title	VDV+Peg-IFN+RBV
Reporting group description:	
VDV+placebo to match TGV+Peg-IFN+RBV for 24 weeks followed by response-guided therapy with Peg-IFN+RBV	
Reporting group title	Peg-IFN+RBV
Reporting group description:	
Placebo to match VDV+placebo to match TGV+Peg-IFN+RBV for 24 weeks followed by Peg-IFN+RBV for 24 weeks	

Serious adverse events	TGV+VDV+Peg-IFN+RBV	VDV+Peg-IFN+RBV	Peg-IFN+RBV
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 119 (2.52%)	3 / 59 (5.08%)	2 / 61 (3.28%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 119 (0.00%)	1 / 59 (1.69%)	0 / 61 (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
Injury, poisoning and procedural complications			
Injury			
subjects affected / exposed	0 / 119 (0.00%)	0 / 59 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Blood and lymphatic system disorders			
Aplastic anaemia			

subjects affected / exposed	1 / 119 (0.84%)	0 / 59 (0.00%)	0 / 61 (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
Febrile neutropenia			
subjects affected / exposed	1 / 119 (0.84%)	0 / 59 (0.00%)	0 / 61 (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
Pancytopenia			
subjects affected / exposed	1 / 119 (0.84%)	0 / 59 (0.00%)	0 / 61 (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
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 119 (0.84%)	0 / 59 (0.00%)	0 / 61 (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
Eye disorders			
Retinal exudates			
subjects affected / exposed	0 / 119 (0.00%)	1 / 59 (1.69%)	0 / 61 (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
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	1 / 119 (0.84%)	0 / 59 (0.00%)	0 / 61 (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
Psychiatric disorders			
Alcoholism			
subjects affected / exposed	0 / 119 (0.00%)	1 / 59 (1.69%)	0 / 61 (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
Bipolar I disorder			

subjects affected / exposed	0 / 119 (0.00%)	1 / 59 (1.69%)	0 / 61 (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
Drug abuse			
subjects affected / exposed	0 / 119 (0.00%)	1 / 59 (1.69%)	0 / 61 (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			
Pneumonia			
subjects affected / exposed	0 / 119 (0.00%)	0 / 59 (0.00%)	1 / 61 (1.64%)
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	TGV+VDV+Peg-IFN+RBV	VDV+Peg-IFN+RBV	Peg-IFN+RBV
Total subjects affected by non-serious adverse events			
subjects affected / exposed	116 / 119 (97.48%)	59 / 59 (100.00%)	59 / 61 (96.72%)
Vascular disorders			
Hot flush			
subjects affected / exposed	2 / 119 (1.68%)	3 / 59 (5.08%)	1 / 61 (1.64%)
occurrences (all)	2	3	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	65 / 119 (54.62%)	29 / 59 (49.15%)	34 / 61 (55.74%)
occurrences (all)	66	29	35
Pyrexia			
subjects affected / exposed	21 / 119 (17.65%)	11 / 59 (18.64%)	14 / 61 (22.95%)
occurrences (all)	27	12	14
Chills			
subjects affected / exposed	18 / 119 (15.13%)	7 / 59 (11.86%)	14 / 61 (22.95%)
occurrences (all)	21	7	15
Irritability			
subjects affected / exposed	18 / 119 (15.13%)	8 / 59 (13.56%)	9 / 61 (14.75%)
occurrences (all)	19	8	9

Injection site reaction			
subjects affected / exposed	13 / 119 (10.92%)	6 / 59 (10.17%)	15 / 61 (24.59%)
occurrences (all)	13	6	16
Influenza like illness			
subjects affected / exposed	13 / 119 (10.92%)	5 / 59 (8.47%)	10 / 61 (16.39%)
occurrences (all)	14	6	11
Pain			
subjects affected / exposed	7 / 119 (5.88%)	4 / 59 (6.78%)	9 / 61 (14.75%)
occurrences (all)	13	4	9
Asthenia			
subjects affected / exposed	6 / 119 (5.04%)	3 / 59 (5.08%)	7 / 61 (11.48%)
occurrences (all)	7	4	7
Chest discomfort			
subjects affected / exposed	2 / 119 (1.68%)	3 / 59 (5.08%)	0 / 61 (0.00%)
occurrences (all)	2	3	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	22 / 119 (18.49%)	9 / 59 (15.25%)	9 / 61 (14.75%)
occurrences (all)	24	10	11
Dyspnoea			
subjects affected / exposed	24 / 119 (20.17%)	4 / 59 (6.78%)	4 / 61 (6.56%)
occurrences (all)	24	4	4
Oropharyngeal pain			
subjects affected / exposed	7 / 119 (5.88%)	3 / 59 (5.08%)	5 / 61 (8.20%)
occurrences (all)	7	3	6
Dyspnoea exertional			
subjects affected / exposed	8 / 119 (6.72%)	1 / 59 (1.69%)	3 / 61 (4.92%)
occurrences (all)	8	1	3
Epistaxis			
subjects affected / exposed	2 / 119 (1.68%)	1 / 59 (1.69%)	4 / 61 (6.56%)
occurrences (all)	2	2	4
Nasal congestion			
subjects affected / exposed	0 / 119 (0.00%)	3 / 59 (5.08%)	1 / 61 (1.64%)
occurrences (all)	0	3	1
Wheezing			

subjects affected / exposed	0 / 119 (0.00%)	0 / 59 (0.00%)	4 / 61 (6.56%)
occurrences (all)	0	0	4
Psychiatric disorders			
Insomnia			
subjects affected / exposed	32 / 119 (26.89%)	16 / 59 (27.12%)	13 / 61 (21.31%)
occurrences (all)	32	17	13
Depression			
subjects affected / exposed	29 / 119 (24.37%)	8 / 59 (13.56%)	12 / 61 (19.67%)
occurrences (all)	29	8	12
Anxiety			
subjects affected / exposed	9 / 119 (7.56%)	11 / 59 (18.64%)	3 / 61 (4.92%)
occurrences (all)	9	12	3
Investigations			
Weight decreased			
subjects affected / exposed	7 / 119 (5.88%)	2 / 59 (3.39%)	5 / 61 (8.20%)
occurrences (all)	7	2	6
Neutrophil count decreased			
subjects affected / exposed	5 / 119 (4.20%)	3 / 59 (5.08%)	1 / 61 (1.64%)
occurrences (all)	6	3	3
Haemoglobin decreased			
subjects affected / exposed	3 / 119 (2.52%)	3 / 59 (5.08%)	0 / 61 (0.00%)
occurrences (all)	3	4	0
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 119 (1.68%)	3 / 59 (5.08%)	0 / 61 (0.00%)
occurrences (all)	2	4	0
White blood cell count decreased			
subjects affected / exposed	2 / 119 (1.68%)	3 / 59 (5.08%)	0 / 61 (0.00%)
occurrences (all)	2	3	0
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 119 (0.84%)	3 / 59 (5.08%)	0 / 61 (0.00%)
occurrences (all)	1	3	0
Nervous system disorders			
Headache			
subjects affected / exposed	56 / 119 (47.06%)	23 / 59 (38.98%)	23 / 61 (37.70%)
occurrences (all)	69	27	32
Dizziness			

subjects affected / exposed	10 / 119 (8.40%)	6 / 59 (10.17%)	8 / 61 (13.11%)
occurrences (all)	10	6	9
Dysgeusia			
subjects affected / exposed	8 / 119 (6.72%)	3 / 59 (5.08%)	5 / 61 (8.20%)
occurrences (all)	8	3	5
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	33 / 119 (27.73%)	15 / 59 (25.42%)	21 / 61 (34.43%)
occurrences (all)	37	21	25
Anaemia			
subjects affected / exposed	26 / 119 (21.85%)	15 / 59 (25.42%)	17 / 61 (27.87%)
occurrences (all)	29	15	20
Leukopenia			
subjects affected / exposed	8 / 119 (6.72%)	3 / 59 (5.08%)	5 / 61 (8.20%)
occurrences (all)	9	5	5
Thrombocytopenia			
subjects affected / exposed	7 / 119 (5.88%)	2 / 59 (3.39%)	2 / 61 (3.28%)
occurrences (all)	7	2	2
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	6 / 119 (5.04%)	3 / 59 (5.08%)	5 / 61 (8.20%)
occurrences (all)	6	3	5
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 119 (0.00%)	3 / 59 (5.08%)	1 / 61 (1.64%)
occurrences (all)	0	3	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	44 / 119 (36.97%)	22 / 59 (37.29%)	19 / 61 (31.15%)
occurrences (all)	49	23	21
Diarrhoea			
subjects affected / exposed	30 / 119 (25.21%)	7 / 59 (11.86%)	10 / 61 (16.39%)
occurrences (all)	35	7	10
Dyspepsia			
subjects affected / exposed	11 / 119 (9.24%)	2 / 59 (3.39%)	5 / 61 (8.20%)
occurrences (all)	11	2	5
Vomiting			

subjects affected / exposed	12 / 119 (10.08%)	3 / 59 (5.08%)	3 / 61 (4.92%)
occurrences (all)	14	4	3
Abdominal pain			
subjects affected / exposed	8 / 119 (6.72%)	3 / 59 (5.08%)	2 / 61 (3.28%)
occurrences (all)	10	3	3
Abdominal pain upper			
subjects affected / exposed	6 / 119 (5.04%)	2 / 59 (3.39%)	4 / 61 (6.56%)
occurrences (all)	6	2	4
Constipation			
subjects affected / exposed	5 / 119 (4.20%)	4 / 59 (6.78%)	3 / 61 (4.92%)
occurrences (all)	5	5	3
Dry mouth			
subjects affected / exposed	4 / 119 (3.36%)	3 / 59 (5.08%)	0 / 61 (0.00%)
occurrences (all)	4	3	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	33 / 119 (27.73%)	9 / 59 (15.25%)	18 / 61 (29.51%)
occurrences (all)	43	12	21
Alopecia			
subjects affected / exposed	23 / 119 (19.33%)	9 / 59 (15.25%)	15 / 61 (24.59%)
occurrences (all)	23	9	15
Pruritus			
subjects affected / exposed	20 / 119 (16.81%)	9 / 59 (15.25%)	11 / 61 (18.03%)
occurrences (all)	23	9	12
Dry skin			
subjects affected / exposed	10 / 119 (8.40%)	3 / 59 (5.08%)	9 / 61 (14.75%)
occurrences (all)	10	3	9
Pruritus generalised			
subjects affected / exposed	5 / 119 (4.20%)	4 / 59 (6.78%)	1 / 61 (1.64%)
occurrences (all)	5	4	1
Rash pruritic			
subjects affected / exposed	5 / 119 (4.20%)	3 / 59 (5.08%)	1 / 61 (1.64%)
occurrences (all)	5	3	1
Rash papular			
subjects affected / exposed	2 / 119 (1.68%)	3 / 59 (5.08%)	3 / 61 (4.92%)
occurrences (all)	2	3	3

Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	3 / 119 (2.52%)	3 / 59 (5.08%)	2 / 61 (3.28%)
occurrences (all)	3	3	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	28 / 119 (23.53%)	11 / 59 (18.64%)	8 / 61 (13.11%)
occurrences (all)	32	11	8
Myalgia			
subjects affected / exposed	22 / 119 (18.49%)	11 / 59 (18.64%)	14 / 61 (22.95%)
occurrences (all)	23	12	14
Back pain			
subjects affected / exposed	9 / 119 (7.56%)	5 / 59 (8.47%)	3 / 61 (4.92%)
occurrences (all)	9	5	3
Muscle spasms			
subjects affected / exposed	7 / 119 (5.88%)	3 / 59 (5.08%)	3 / 61 (4.92%)
occurrences (all)	7	3	3
Infections and infestations			
Sinusitis			
subjects affected / exposed	6 / 119 (5.04%)	2 / 59 (3.39%)	4 / 61 (6.56%)
occurrences (all)	8	3	5
Upper respiratory tract infection			
subjects affected / exposed	4 / 119 (3.36%)	3 / 59 (5.08%)	5 / 61 (8.20%)
occurrences (all)	5	3	5
Bronchitis			
subjects affected / exposed	8 / 119 (6.72%)	0 / 59 (0.00%)	1 / 61 (1.64%)
occurrences (all)	8	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	23 / 119 (19.33%)	8 / 59 (13.56%)	11 / 61 (18.03%)
occurrences (all)	23	8	12

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 November 2010	Protocol was amended to limit to the number of genotype 1a and 1b subjects to no more than 70% of subjects, to include a confirmatory assessment of plasma HCV RNA within approximately 2 weeks in such cases, and to prohibit the use of Pgp substrates with narrow therapeutic indices, including digoxin and colchicine; to allow for an earlier DMC assessment of subject safety and study integrity, the protocol was amended to conduct this initial DMC review after the first 40 subjects enrolled had completed Week 4 of the study.
15 September 2011	In consultation with the FDA, discontinued dosing of tegobuvir when given in combination with Peg-IFN+RBV and another DAA across all active Gilead studies.

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: