Clinical trial results:
A Phase 2b, Randomized, Double-Blind, Placebo-Controlled Trial Comparing 24 or 48 Weeks of GS-9190, in Combination with Peginterferon Alfa 2a and Ribavirin, to 48 Weeks of Peginterferon Alfa 2a and Ribavirin for the Treatment of Genotype-1 Chronic Hepatitis C Virus (HCV) Infection (GS-US-196-0103)

Summary

EudraCT number	2008-004527-31
Trial protocol	IE GB DE BE
Global end of trial date	05 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-196-0103

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00743795
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	05 September 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 September 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study compared the antiviral activity, safety, and tolerability of tegobuvir (TGV; formerly GS-9190) versus placebo, in combination with peginterferon alfa 2a (PEG) and ribavirin (RBV) for the treatment of chronic genotype 1 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	07 October 2008
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 31
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	Germany: 11
Country: Number of subjects enrolled	Ireland: 5
Country: Number of subjects enrolled	Puerto Rico: 8
Country: Number of subjects enrolled	United States: 186
Worldwide total number of subjects	252
EEA total number of subjects	58

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)	249
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in the United States and Europe. The first participant was screened on 07 October 2008. The last study visit occurred on 05 September 2013.

Pre-assignment

Screening details:

Participants were evaluated at a screening visit, and eligible participants were randomized at a 1:2:1 ratio into 1 of 3 treatment groups.

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	Placebo (Group 1)

Arm description:

Placebo to match tegobuvir (TGV) + peginterferon alfa 2a (PEG) + ribavirin (RBV) for 48 weeks

Arm type	Placebo
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 tegobuvir capsules administered orally twice daily

Investigational medicinal product name	Peginterferon alfa 2a
Investigational medicinal product code	
Other name	Pegasys®
Pharmaceutical forms	Suspension for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Peginterferon alfa 2a (PEG) 180 µg administered subcutaneously weekly as 180 µg/0.5 mL prefilled syringes

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

Dosage and administration details:

Ribavirin (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	TGV (Group 2)

Arm description:

TGV+PEG+RBV for 48 weeks

Arm type	Experimental
Investigational medicinal product name	Tegobuvir
Investigational medicinal product code	
Other name	GS-9190
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Tegobuvir (TGV) 40 mg capsules administered orally twice daily

Investigational medicinal product name	Peginterferon alfa 2a
Investigational medicinal product code	
Other name	Pegasys®
Pharmaceutical forms	Suspension for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Peginterferon alfa 2a (PEG) 180 µg administered subcutaneously weekly as 180 µg/0.5 mL prefilled syringes

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

Dosage and administration details:

Ribavirin (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	TGV Response-Guided Therapy (Group 3)

Arm description:

TGV+PEG+RBV for 24 or 48 weeks; Participants who had HCV RNA < 25 IU/mL at Week 4 and undetectable HCV RNA (< 10 IU/mL) at Week 12 through Week 24 stopped all study drugs at Week 24.

Arm type	Experimental
Investigational medicinal product name	Tegobuvir
Investigational medicinal product code	
Other name	GS-9190
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Tegobuvir (TGV) 40 mg capsules administered orally twice daily

Investigational medicinal product name	Peginterferon alfa 2a
Investigational medicinal product code	
Other name	Pegasys®
Pharmaceutical forms	Suspension for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Peginterferon alfa 2a (PEG) 180 µg administered subcutaneously weekly as 180 µg/0.5 mL prefilled syringes

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

Dosage and administration details:

Ribavirin (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 (Group 1)	TGV (Group 2)	TGV Response-Guided Therapy (Group 3)
Started	64	126	62
Completed	34	63	32
Not completed	30	63	30
Safety, tolerability, or efficacy reasons	26	53	25
Lost to follow-up	2	4	3
Withdrew consent	1	5	1
Investigator's discretion	1	1	1

Baseline characteristics

Reporting groups

Reporting group title	Overall study

Reporting group description: -

Reporting group values	Overall study	Total	
Number of subjects	252	252	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	47		
standard deviation	± 10.3	-	
Gender categorical Units: Subjects			
Female	100	100	
Male	152	152	
Race Units: Subjects			
White	215	215	
Black	20	20	
Asian	6	6	
Other	6	6	
American Indian or Alaska Native	4	4	
Native Hawaiian or Pacific Islander	1	1	
Ethnicity Units: Subjects			
Non-Hispanic/Latino	210	210	
Hispanic/Latino	42	42	
Genotype Units: Subjects			
1a	143	143	
1b	108	108	
6e	1	1	
HCV RNA Units: log10 IU/mL			
arithmetic mean	6.3		
standard deviation	± 0.73	-	

Subject analysis sets

Subject analysis set title	TGV
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants in Groups 2 and 3 who received TGV+PEG+RBV for 24 or 48 weeks were included.

Subject analysis set title	Placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants in Group 1 who received placebo to match TGV+PEG+RBV for 48 weeks were included.

Reporting group values	TGV	Placebo	
Number of subjects	188	64	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	47	47	
standard deviation	± 10.4	± 10	
Gender categorical Units: Subjects			
Female	69	31	
Male	119	33	
Race Units: Subjects			
White	160	55	
Black	15	5	
Asian	5	1	
Other	4	2	
American Indian or Alaska Native	4	0	
Native Hawaiian or Pacific Islander	0	1	
Ethnicity Units: Subjects			
Non-Hispanic/Latino	156	54	
Hispanic/Latino	32	10	
Genotype Units: Subjects			
1a	106	37	
1b	81	27	
6e	1	0	
HCV RNA Units: log10 IU/mL			
arithmetic mean	6.3	6.3	
standard deviation	± 0.73	± 0.73	

End points

End points reporting groups

Reporting group title	Placebo (Group 1)
Reporting group description:	
Placebo to match tegobuvir (TGV) + peginterferon alfa 2a (PEG) + ribavirin (RBV) for 48 weeks	

Reporting group title	TGV (Group 2)
Reporting group description:	
TGV+PEG+RBV for 48 weeks	

Reporting group title	TGV Response-Guided Therapy (Group 3)
Reporting group description:	
TGV+PEG+RBV for 24 or 48 weeks; Participants who had HCV RNA < 25 IU/mL at Week 4 and undetectable HCV RNA (< 10 IU/mL) at Week 12 through Week 24 stopped all study drugs at Week 24.	

Subject analysis set title	TGV
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants in Groups 2 and 3 who received TGV+PEG+RBV for 24 or 48 weeks were included.	

Subject analysis set title	Placebo
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants in Group 1 who received placebo to match TGV+PEG+RBV for 48 weeks were included.	

Primary: Percentage of participants with complete early virologic response (cEVR)

End point title	Percentage of participants with complete early virologic response (cEVR)
End point description:	
cEVR was defined as undetectable HCV RNA at Week 12.	
End point type	Primary
End point timeframe:	
Week 12	

End point values	TGV	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	187	64		
Units: percentage of participants				
number (not applicable)	66.8	46.9		

Statistical analyses

Statistical analysis title	P-value between TGV vs placebo
Comparison groups	TGV v Placebo
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002 [1]
Method	Cochran-Mantel-Haenszel

Notes:

[1] - P-value was determined from the Cochran-Mantel-Haenszel (CMH) test statistic for stratified proportions. Stratification was based on plasma HCV RNA level (< or ≥ 400,000 IU/mL at screening).

Primary: Percentage of participants who discontinued study drug due to an adverse event

End point title	Percentage of participants who discontinued study drug due to an adverse event[2]

End point description:

End point type	Primary

End point timeframe:

Up to 48 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 hypothesis testing was planned or performed for this endpoint.

End point values	TGV	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	188	64		
Units: percentage of participants				
number (not applicable)	16.5	15.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with rapid virologic response (RVR) at Week 4

End point title	Percentage of participants with rapid virologic response (RVR) at Week 4

End point description:

RVR was defined as HCV RNA < 25 IU/mL.

End point type	Secondary

End point timeframe:

Week 4

End point values	TGV	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	187	64		
Units: percentage of participants				
number (not applicable)	54.5	20.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with complete rapid virologic response (cRVR)

End point title	Percentage of participants with complete rapid virologic response (cRVR)

End point description:

cRVR was defined as HCV RNA < 25 IU/mL at Week 4 and < 10 IU/mL at Weeks 12, 20, and 24.

End point type	Secondary

End point timeframe:

Up to 24 weeks

End point values	TGV	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	187	64		
Units: percentage of participants				
number (not applicable)	46.5	18.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with virological suppression below the limit of assay detection (ie, HCV RNA < 10 IU/mL) at Weeks 24 and 48

End point title	Percentage of participants with virological suppression below the limit of assay detection (ie, HCV RNA < 10 IU/mL) at Weeks 24 and 48

End point description:

End point type	Secondary

End point timeframe:

Weeks 24 and 48

End point values	TGV	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	187	64		
Units: percentage of participants				
number (not applicable)				
Week 24	67.9	70.3		
Week 48	63.1	65.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with sustained virologic response (SVR)

End point title	Percentage of participants with sustained virologic response (SVR)

End point description:

SVR was defined as HCV RNA < 10 IU/mL 24 weeks following the last dose of study drug.

End point type	Secondary

End point timeframe:

Posttreatment Week 24

End point values	TGV	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	187	64		
Units: percentage of participants				
number (not applicable)	55.6	56.3		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to 48 weeks plus 30 days	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	10
Reporting groups	
Reporting group title	Placebo (Group 1)
Reporting group description: Placebo to match TGV+PEG+RBV for 48 weeks	
Reporting group title	TGV (Group 2)
Reporting group description: TGV+PEG+RBV for 48 weeks	
Reporting group title	TGV (Group 3, 48 weeks)
Reporting group description: TGV+PEG+RBV for 48 weeks	
Reporting group title	TGV (Group 3, 24 weeks)
Reporting group description: TGV+PEG+RBV for 24 weeks; Participants in Group 3 who had HCV RNA < 25 IU/mL at Week 4 and undetectable HCV RNA (< 10 IU/mL) at Week 12 through Week 24 stopped all study drugs at Week 24.	

Serious adverse events	Placebo (Group 1)	TGV (Group 2)	TGV (Group 3, 48 weeks)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 64 (4.69%)	5 / 126 (3.97%)	4 / 37 (10.81%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm malignant			
subjects affected / exposed	0 / 64 (0.00%)	0 / 126 (0.00%)	1 / 37 (2.70%)
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			
Crush injury			
subjects affected / exposed	0 / 64 (0.00%)	1 / 126 (0.79%)	0 / 37 (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
Femur fracture			

subjects affected / exposed	1 / 64 (1.56%)	0 / 126 (0.00%)	0 / 37 (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
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 64 (0.00%)	1 / 126 (0.79%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 64 (0.00%)	1 / 126 (0.79%)	0 / 37 (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
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 64 (1.56%)	0 / 126 (0.00%)	0 / 37 (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
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 64 (0.00%)	1 / 126 (0.79%)	0 / 37 (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
Eye disorders			
Retinal vein occlusion			
subjects affected / exposed	0 / 64 (0.00%)	0 / 126 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Drug abuser			
subjects affected / exposed	1 / 64 (1.56%)	0 / 126 (0.00%)	0 / 37 (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
Respiratory, thoracic and mediastinal disorders			

Asthma			
subjects affected / exposed	0 / 64 (0.00%)	1 / 126 (0.79%)	0 / 37 (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
Psychiatric disorders			
Disorientation			
subjects affected / exposed	0 / 64 (0.00%)	0 / 126 (0.00%)	1 / 37 (2.70%)
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 / 64 (1.56%)	0 / 126 (0.00%)	0 / 37 (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
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	0 / 64 (0.00%)	0 / 126 (0.00%)	1 / 37 (2.70%)
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			
Bronchitis			
subjects affected / exposed	0 / 64 (0.00%)	1 / 126 (0.79%)	0 / 37 (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
Pneumonia			
subjects affected / exposed	0 / 64 (0.00%)	1 / 126 (0.79%)	0 / 37 (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
Viral infection			
subjects affected / exposed	0 / 64 (0.00%)	0 / 126 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	1 / 64 (1.56%)	0 / 126 (0.00%)	0 / 37 (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

Serious adverse events	TGV (Group 3, 24 weeks)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 25 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm malignant			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Crush injury			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Femur fracture			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 25 (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 / 25 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Retinal vein occlusion			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Social circumstances			
Drug abuser			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Disorientation			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Suicidal ideation			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			

Muscular weakness			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 25 (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	Placebo (Group 1)	TGV (Group 2)	TGV (Group 3, 48 weeks)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	60 / 64 (93.75%)	120 / 126 (95.24%)	35 / 37 (94.59%)
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 64 (7.81%)	10 / 126 (7.94%)	1 / 37 (2.70%)
occurrences (all)	5	10	1
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed	27 / 64 (42.19%)	52 / 126 (41.27%)	17 / 37 (45.95%)
occurrences (all)	27	56	17
Influenza like illness			
subjects affected / exposed	13 / 64 (20.31%)	34 / 126 (26.98%)	2 / 37 (5.41%)
occurrences (all)	14	39	2
Pyrexia			
subjects affected / exposed	4 / 64 (6.25%)	36 / 126 (28.57%)	10 / 37 (27.03%)
occurrences (all)	5	43	11
Irritability			
subjects affected / exposed	13 / 64 (20.31%)	24 / 126 (19.05%)	10 / 37 (27.03%)
occurrences (all)	15	24	11
Chills			
subjects affected / exposed	7 / 64 (10.94%)	15 / 126 (11.90%)	13 / 37 (35.14%)
occurrences (all)	9	16	14
Asthenia			
subjects affected / exposed	2 / 64 (3.13%)	18 / 126 (14.29%)	2 / 37 (5.41%)
occurrences (all)	2	20	3
Pain			
subjects affected / exposed	6 / 64 (9.38%)	11 / 126 (8.73%)	4 / 37 (10.81%)
occurrences (all)	6	11	4
Injection site erythema			
subjects affected / exposed	2 / 64 (3.13%)	8 / 126 (6.35%)	8 / 37 (21.62%)
occurrences (all)	2	8	8
Injection site reaction			
subjects affected / exposed	3 / 64 (4.69%)	8 / 126 (6.35%)	1 / 37 (2.70%)
occurrences (all)	3	9	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 64 (10.94%)	25 / 126 (19.84%)	8 / 37 (21.62%)
occurrences (all)	7	25	9
Dyspnoea			
subjects affected / exposed	11 / 64 (17.19%)	16 / 126 (12.70%)	4 / 37 (10.81%)
occurrences (all)	11	16	4
Dyspnoea exertional			

subjects affected / exposed	4 / 64 (6.25%)	12 / 126 (9.52%)	2 / 37 (5.41%)
occurrences (all)	4	12	2
Pharyngolaryngeal pain			
subjects affected / exposed	3 / 64 (4.69%)	10 / 126 (7.94%)	2 / 37 (5.41%)
occurrences (all)	3	10	2
Productive cough			
subjects affected / exposed	3 / 64 (4.69%)	8 / 126 (6.35%)	2 / 37 (5.41%)
occurrences (all)	3	8	2
Nasal congestion			
subjects affected / exposed	1 / 64 (1.56%)	7 / 126 (5.56%)	0 / 37 (0.00%)
occurrences (all)	1	7	0
Respiratory tract congestion			
subjects affected / exposed	1 / 64 (1.56%)	3 / 126 (2.38%)	2 / 37 (5.41%)
occurrences (all)	1	3	2
Increased upper airway secretion			
subjects affected / exposed	0 / 64 (0.00%)	0 / 126 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Psychiatric disorders			
Insomnia			
subjects affected / exposed	20 / 64 (31.25%)	38 / 126 (30.16%)	13 / 37 (35.14%)
occurrences (all)	20	40	14
Depression			
subjects affected / exposed	13 / 64 (20.31%)	28 / 126 (22.22%)	9 / 37 (24.32%)
occurrences (all)	13	29	9
Anxiety			
subjects affected / exposed	12 / 64 (18.75%)	20 / 126 (15.87%)	5 / 37 (13.51%)
occurrences (all)	13	21	5
Investigations			
Weight decreased			
subjects affected / exposed	7 / 64 (10.94%)	12 / 126 (9.52%)	3 / 37 (8.11%)
occurrences (all)	7	12	3
Nervous system disorders			
Headache			
subjects affected / exposed	20 / 64 (31.25%)	56 / 126 (44.44%)	15 / 37 (40.54%)
occurrences (all)	25	64	31
Dizziness			

subjects affected / exposed	6 / 64 (9.38%)	12 / 126 (9.52%)	6 / 37 (16.22%)
occurrences (all)	6	14	7
Dysgeusia			
subjects affected / exposed	2 / 64 (3.13%)	12 / 126 (9.52%)	1 / 37 (2.70%)
occurrences (all)	2	12	1
Migraine			
subjects affected / exposed	2 / 64 (3.13%)	4 / 126 (3.17%)	1 / 37 (2.70%)
occurrences (all)	2	4	1
Hypoaesthesia			
subjects affected / exposed	1 / 64 (1.56%)	3 / 126 (2.38%)	2 / 37 (5.41%)
occurrences (all)	1	3	2
Paraesthesia			
subjects affected / exposed	1 / 64 (1.56%)	2 / 126 (1.59%)	0 / 37 (0.00%)
occurrences (all)	1	3	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	19 / 64 (29.69%)	40 / 126 (31.75%)	8 / 37 (21.62%)
occurrences (all)	23	58	12
Anaemia			
subjects affected / exposed	20 / 64 (31.25%)	33 / 126 (26.19%)	6 / 37 (16.22%)
occurrences (all)	25	36	6
Lymphopenia			
subjects affected / exposed	1 / 64 (1.56%)	4 / 126 (3.17%)	2 / 37 (5.41%)
occurrences (all)	1	4	2
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 64 (1.56%)	4 / 126 (3.17%)	2 / 37 (5.41%)
occurrences (all)	1	4	2
Eye pain			
subjects affected / exposed	0 / 64 (0.00%)	1 / 126 (0.79%)	3 / 37 (8.11%)
occurrences (all)	0	1	4
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	14 / 64 (21.88%)	27 / 126 (21.43%)	15 / 37 (40.54%)
occurrences (all)	17	27	16
Diarrhoea			

subjects affected / exposed	10 / 64 (15.63%)	25 / 126 (19.84%)	8 / 37 (21.62%)
occurrences (all)	10	28	9
Dyspepsia			
subjects affected / exposed	8 / 64 (12.50%)	7 / 126 (5.56%)	2 / 37 (5.41%)
occurrences (all)	10	8	2
Vomiting			
subjects affected / exposed	2 / 64 (3.13%)	8 / 126 (6.35%)	5 / 37 (13.51%)
occurrences (all)	2	10	6
Abdominal pain upper			
subjects affected / exposed	3 / 64 (4.69%)	9 / 126 (7.14%)	2 / 37 (5.41%)
occurrences (all)	3	10	2
Constipation			
subjects affected / exposed	3 / 64 (4.69%)	7 / 126 (5.56%)	3 / 37 (8.11%)
occurrences (all)	3	7	3
Dry mouth			
subjects affected / exposed	2 / 64 (3.13%)	8 / 126 (6.35%)	2 / 37 (5.41%)
occurrences (all)	2	8	2
Gastroesophageal reflux disease			
subjects affected / exposed	2 / 64 (3.13%)	8 / 126 (6.35%)	3 / 37 (8.11%)
occurrences (all)	2	8	3
Abdominal pain			
subjects affected / exposed	2 / 64 (3.13%)	4 / 126 (3.17%)	3 / 37 (8.11%)
occurrences (all)	2	4	3
Stomatitis			
subjects affected / exposed	2 / 64 (3.13%)	5 / 126 (3.97%)	2 / 37 (5.41%)
occurrences (all)	2	5	2
Cheilitis			
subjects affected / exposed	0 / 64 (0.00%)	2 / 126 (1.59%)	2 / 37 (5.41%)
occurrences (all)	0	2	2
Tongue discolouration			
subjects affected / exposed	0 / 64 (0.00%)	1 / 126 (0.79%)	2 / 37 (5.41%)
occurrences (all)	0	1	2
Pruritus ani			
subjects affected / exposed	0 / 64 (0.00%)	0 / 126 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Skin and subcutaneous tissue disorders			

Alopecia			
subjects affected / exposed	10 / 64 (15.63%)	34 / 126 (26.98%)	11 / 37 (29.73%)
occurrences (all)	11	34	11
Pruritus			
subjects affected / exposed	11 / 64 (17.19%)	29 / 126 (23.02%)	10 / 37 (27.03%)
occurrences (all)	11	32	10
Rash			
subjects affected / exposed	11 / 64 (17.19%)	24 / 126 (19.05%)	10 / 37 (27.03%)
occurrences (all)	12	31	11
Dry skin			
subjects affected / exposed	6 / 64 (9.38%)	13 / 126 (10.32%)	3 / 37 (8.11%)
occurrences (all)	6	13	3
Eczema			
subjects affected / exposed	3 / 64 (4.69%)	7 / 126 (5.56%)	1 / 37 (2.70%)
occurrences (all)	3	7	1
Night sweats			
subjects affected / exposed	4 / 64 (6.25%)	2 / 126 (1.59%)	1 / 37 (2.70%)
occurrences (all)	4	2	1
Rash generalised			
subjects affected / exposed	4 / 64 (6.25%)	0 / 126 (0.00%)	1 / 37 (2.70%)
occurrences (all)	4	0	1
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	6 / 64 (9.38%)	27 / 126 (21.43%)	7 / 37 (18.92%)
occurrences (all)	6	28	10
Arthralgia			
subjects affected / exposed	5 / 64 (7.81%)	20 / 126 (15.87%)	5 / 37 (13.51%)
occurrences (all)	5	21	7
Back pain			
subjects affected / exposed	5 / 64 (7.81%)	19 / 126 (15.08%)	2 / 37 (5.41%)
occurrences (all)	5	20	2
Muscle spasms			
subjects affected / exposed	3 / 64 (4.69%)	8 / 126 (6.35%)	3 / 37 (8.11%)
occurrences (all)	3	8	4
Muscular weakness			

subjects affected / exposed	0 / 64 (0.00%)	2 / 126 (1.59%)	1 / 37 (2.70%)
occurrences (all)	0	2	1
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	2 / 64 (3.13%)	6 / 126 (4.76%)	5 / 37 (13.51%)
occurrences (all)	3	6	5
Urinary tract infection			
subjects affected / exposed	3 / 64 (4.69%)	6 / 126 (4.76%)	4 / 37 (10.81%)
occurrences (all)	3	7	4
Bronchitis			
subjects affected / exposed	2 / 64 (3.13%)	5 / 126 (3.97%)	2 / 37 (5.41%)
occurrences (all)	2	6	2
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	8 / 64 (12.50%)	14 / 126 (11.11%)	2 / 37 (5.41%)
occurrences (all)	8	16	2
Decreased appetite			
subjects affected / exposed	2 / 64 (3.13%)	4 / 126 (3.17%)	3 / 37 (8.11%)
occurrences (all)	2	4	3

Non-serious adverse events	TGV (Group 3, 24 weeks)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 25 (92.00%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	3		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	10 / 25 (40.00%)		
occurrences (all)	11		
Influenza like illness			
subjects affected / exposed	7 / 25 (28.00%)		
occurrences (all)	8		
Pyrexia			

subjects affected / exposed	5 / 25 (20.00%)		
occurrences (all)	6		
Irritability			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	4		
Chills			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Asthenia			
subjects affected / exposed	4 / 25 (16.00%)		
occurrences (all)	4		
Pain			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Injection site erythema			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	3		
Injection site reaction			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	10 / 25 (40.00%)		
occurrences (all)	10		
Dyspnoea			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	3		
Dyspnoea exertional			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Pharyngolaryngeal pain			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	3		
Productive cough			

subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0		
Nasal congestion subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0		
Respiratory tract congestion subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0		
Increased upper airway secretion subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	5 / 25 (20.00%) 5		
Depression subjects affected / exposed occurrences (all)	2 / 25 (8.00%) 2		
Anxiety subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0		
Investigations Weight decreased subjects affected / exposed occurrences (all)	4 / 25 (16.00%) 4		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	9 / 25 (36.00%) 11		
Dizziness subjects affected / exposed occurrences (all)	3 / 25 (12.00%) 3		
Dysgeusia subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		
Migraine			

subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Hypoaesthesia			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Paraesthesia			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	6 / 25 (24.00%)		
occurrences (all)	6		
Anaemia			
subjects affected / exposed	5 / 25 (20.00%)		
occurrences (all)	6		
Lymphopenia			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Eye pain			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	9 / 25 (36.00%)		
occurrences (all)	13		
Diarrhoea			
subjects affected / exposed	4 / 25 (16.00%)		
occurrences (all)	7		
Dyspepsia			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Vomiting			

subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	3		
Abdominal pain upper			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Dry mouth			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Gastroesophageal reflux disease			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	4		
Stomatitis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Cheilitis			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Tongue discolouration			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Pruritus ani			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	9 / 25 (36.00%)		
occurrences (all)	9		
Pruritus			
subjects affected / exposed	6 / 25 (24.00%)		
occurrences (all)	6		

Rash			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	3		
Dry skin			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Eczema			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Night sweats			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Rash generalised			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	7 / 25 (28.00%)		
occurrences (all)	8		
Arthralgia			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	3		
Back pain			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Muscle spasms			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	4		
Muscular weakness			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Urinary tract infection			

subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Bronchitis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	5 / 25 (20.00%)		
occurrences (all)	5		
Decreased appetite			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 October 2008	Subjects up to 70 years of age were allowed to enroll if all other eligibility criteria were met, sample size calculation was revised based on updated assumptions, and sustained virologic response (SVR) was removed as a coprimary endpoint and added as a secondary endpoint to better reflect the objectives of the study.
20 March 2009	The study exceeded the initial planned enrollment by approximately 25% and the protocol was amended to allow enrollment of 248 subjects.
29 April 2009	The HCV RNA stopping criteria for subjects in Arm 3 was updated to avoid ambiguity since there were some inconsistencies historically on the lower limit of detection reported for rapid virologic response (RVR). Subjects in Arm 3 stopped all therapy at Week 24 if they had HCV RNA < 25 IU/mL at Week 4 and undetectable HCV RNA (< 10 IU/mL) at Week 12 and maintained through Week 24.

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: