Clinical trial results:
A Phase 2, Multicenter, Open-Label Study to Evaluate the Efficacy and Safety of Sofosbuvir/Velpatasvir Fixed-Dose Combination and Ribavirin for 12 Weeks in Subjects with Chronic HCV Infection and Child-Pugh-Turcotte Class C Cirrhosis

Summary

EudraCT number	2016-003066-10
Trial protocol	FR
Global end of trial date	12 December 2018

Results information

Result version number	v1 (current)
This version publication date	25 October 2019
First version publication date	25 October 2019

Trial information

Trial identification

Sponsor protocol code	GS-US-342-4022

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02994056
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	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com
Scientific contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@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	12 December 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 September 2018
Global end of trial reached?	Yes
Global end of trial date	12 December 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study were to evaluate the efficacy, safety, and tolerability of the treatment with sofosbuvir velpatasvir (SOF/VEL) fixed-dose combination (FDC) with ribavirin (RBV) for 12 weeks in participants with chronic hepatitis C virus (HCV) infection and Child-Pugh-Turcotte (CPT) Class C cirrhosis.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.
This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 January 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	United States: 26
Worldwide total number of subjects	32
EEA total number of subjects	6

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)	30
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in the United States and France. The first participant was screened on 23 January 2017. The last study visit occurred on 12 December 2018.

Pre-assignment

Screening details:

73 participants were screened.

Period 1

Period 1 title	SOF/VEL+ RBV (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	SOF/VEL+ RBV (Total)

Arm description:

SOF/VEL (400/100 mg) FDC tablet once daily + RBV tablet (600-1200 mg based on weight) divided twice daily for 12 weeks in participants with HCV infection and CPT Class C cirrhosis

Arm type	Experimental
Investigational medicinal product name	Sofosbuvir/velpatasvir
Investigational medicinal product code	
Other name	SOF/VEL; Epclusa®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

400/100 mg FDC orally once daily

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

Dosage and administration details:

600-1200 mg based on weight divided twice daily

Number of subjects in period 1	SOF/VEL+ RBV (Total)
Started	32
Completed	23
Not completed	9
Withdrew Consent	1
Death	8

Baseline characteristics

Reporting groups	
Reporting group title	SOF/VEL+ RBV (Total)
Reporting group description:	
SOF/VEL (400/100 mg) FDC tablet once daily + RBV tablet (600-1200 mg based on weight) divided twice daily for 12 weeks in participants with HCV infection and CPT Class C cirrhosis	

Reporting group values	SOF/VEL+ RBV (Total)	Total	
Number of subjects	32	32	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	55		
standard deviation	± 7.0	-	
Gender categorical Units: Subjects			
Female	6	6	
Male	26	26	
Ethnicity Units: Subjects			
Hispanic or Latino	7	7	
Not Hispanic or Latino	19	19	
Unkown or Not Reported	6	6	
Race Units: Subjects			
American Indian or Alaska Native	1	1	
Black or African American Native	6	6	
White	18	18	
Not Permitted	6	6	
Other	1	1	
HCV RNA Category Units: Subjects			
< 800,000 IU/mL	23	23	
≥ 800,000 IU/mL	9	9	
IL28B			
The CC, CT, and TT alleles are different forms of the IL28b gene.			
Units: Subjects			
CC	15	15	
CT	14	14	
TT	3	3	
Child-Pugh-Turcotte Class			
CPT is a chronic liver disease classification system. Classes include CPT Class A, CPT Class B, and CPT Class C, in order of greater disease severity.			
Units: Subjects			
CPT B [7-9]	9	9	
CPT C [10-15]	23	23	

Model for End Stage Liver Disease (MELD) Score Category			
MELD score is a chronic liver disease severity scoring system. Scores can range from 6 to 40, with higher scores indicating greater disease severity.			
Units: Subjects			
10-15 MELD Score	13	13	
16-20 MELD Score	17	17	
21-25 MELD Score	2	2	
HCV RNA			
Units: log10 IU/mL			
arithmetic mean	5.2		
standard deviation	± 1.19	-	

End points

End points reporting groups

Reporting group title	SOF/VEL+ RBV (Total)
Reporting group description:	
SOF/VEL (400/100 mg) FDC tablet once daily + RBV tablet (600-1200 mg based on weight) divided twice daily for 12 weeks in participants with HCV infection and CPT Class C cirrhosis	
Subject analysis set title	SOF/VEL+ RBV (GT-1)
Subject analysis set type	Full analysis
Subject analysis set description:	
SOF/VEL (400/100 mg) FDC tablet once daily + RBV tablet (600-1200 mg based on weight) divided twice daily for 12 weeks in participants with genotype 1 (GT-1) HCV infection and CPT Class C cirrhosis	
Subject analysis set title	SOF/VEL+ RBV (GT-2)
Subject analysis set type	Full analysis
Subject analysis set description:	
SOF/VEL (400/100 mg) FDC tablet once daily + RBV tablet (600-1200 mg based on weight) divided twice daily for 12 weeks in participants with genotype 2 (GT-2) HCV infection and CPT Class C cirrhosis	
Subject analysis set title	SOF/VEL+ RBV (GT-3)
Subject analysis set type	Full analysis
Subject analysis set description:	
SOF/VEL (400/100 mg) FDC tablet once daily + RBV tablet (600-1200 mg based on weight) divided twice daily for 12 weeks in participants with genotype 3 (GT-3) HCV infection and CPT Class C cirrhosis	

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

End point title	Percentage of Participants With Sustained Virologic Response (SVR) 12 Weeks After Discontinuation of Therapy (SVR12)[1]
End point description:	
SVR12 was defined as HCV RNA < the lower limit of quantitation (LLOQ; ie, 15 IU/mL) at 12 weeks after stopping study treatment. The Full Analysis Set included all enrolled participants who took at least 1 dose of study drug.	
End point type	Primary
End point timeframe:	
Posttreatment Week 12	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical comparison was planned or performed.

End point values	SOF/VEL+ RBV (Total)	SOF/VEL+ RBV (GT-1)	SOF/VEL+ RBV (GT-2)	SOF/VEL+ RBV (GT-3)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	32	18	5	7
Units: Percentage of participants				
number (confidence interval 95%)	78.1 (60.0 to 90.7)	72.2 (46.5 to 90.3)	80.0 (28.4 to 99.5)	85.7 (42.1 to 99.6)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Permanently Discontinued Study Drug (SOF/VEL or RBV) Due to an Adverse Event

End point title	Percentage of Participants Who Permanently Discontinued Study Drug (SOF/VEL or RBV) Due to an Adverse Event[2]

End point description:

The Safety Analysis Set included all participants who took at least 1 dose of study drug.

End point type	Primary

End point timeframe:

First dose date up to Week 12

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical comparison was planned or performed.

End point values	SOF/VEL+ RBV (Total)			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: percentage of participants				
number (not applicable)				
Discontinuation of SOF/VEL	6.3			
Discontinuation of RBV	21.9			

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Participants With Sustained Virologic Response 4 Weeks After Discontinuation of Therapy (SVR4)

End point description:

SVR4 was defined as HCV RNA < LLOQ at 4 weeks after stopping study treatment. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Posttreatment Week 4

End point values	SOF/VEL+ RBV (Total)	SOF/VEL+ RBV (GT-1)	SOF/VEL+ RBV (GT-2)	SOF/VEL+ RBV (GT-3)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	32	18	5	7
Units: Percentage of participants				
number (confidence interval 95%)	87.5 (71.0 to 96.5)	88.9 (65.3 to 98.6)	80.0 (28.4 to 99.5)	85.7 (42.1 to 99.6)

Statistical analyses

No statistical analyses for this end point

Secondary: 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:

SVR4 was defined as HCV RNA < LLOQ 24 weeks after stopping study treatment. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Posttreatment Week 24

End point values	SOF/VEL+ RBV (Total)	SOF/VEL+ RBV (GT-1)	SOF/VEL+ RBV (GT-2)	SOF/VEL+ RBV (GT-3)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	32	18	5	7
Units: Percentage of participants				
number (confidence interval 95%)	75.0 (56.6 to 88.5)	72.2 (46.5 to 90.3)	80.0 (28.4 to 99.5)	71.4 (29.0 to 96.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HCV RNA < LLOQ While on Study Treatment

End point title	Percentage of Participants With HCV RNA < LLOQ While on Study Treatment

End point description:

Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Weeks 2, 4, 8, and 12

End point values	SOF/VEL+ RBV (Total)	SOF/VEL+ RBV (GT-1)	SOF/VEL+ RBV (GT-2)	SOF/VEL+ RBV (GT-3)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	32	18	5	7
Units: Percentage of participants				
number (confidence interval 95%)				
Week 2 (N = 32, 18, 5, 7)	43.8 (26.4 to 62.3)	38.9 (17.3 to 64.3)	0 (0.0 to 52.2)	71.4 (29.0 to 96.3)
Week 4 (N = 29, 16, 4, 7)	96.6 (82.2 to 99.9)	100.0 (79.4 to 100.0)	75.0 (19.4 to 99.4)	100.0 (59.0 to 100.0)

Week 8 (N = 29, 16, 4, 7)	100.0 (88.1 to 100.0)	100.0 (79.4 to 100.0)	100.0 (39.8 to 100.0)	100.0 (59.0 to 100.0)
Week 12 (N = 29, 16, 4, 7)	100.0 (88.1 to 100.0)	100.0 (79.4 to 100.0)	100.0 (39.8 to 100.0)	100.0 (59.0 to 100.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Improved and Worsened Child-Pugh-Turcotte (CPT) Class

End point title	Percentage of Participants With Improved and Worsened Child-Pugh-Turcotte (CPT) Class

End point description:

CPT is a chronic liver disease classification system. Classes include CPT Class A, CPT Class B, and CPT Class C, in order of greater disease severity. Participants with improved CPT class was defined as having Class C at Baseline and Class B or A at Posttreatment Week 24 or Class B at Baseline and Class A at Posttreatment Week 24. Participants with worsened CPT class was defined as having Class A at Baseline and Class B or C at Posttreatment Week 24 or Class B at Baseline and Class C at Posttreatment Week 24. Participants with no change CPT class was defined as having CPT Class same between Baseline and Posttreatment Week 24.

End point type	Secondary

End point timeframe:

Baseline to Posttreatment Week 24

End point values	SOF/VEL+ RBV (Total)			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: Percentage of participants				
number (not applicable)				
Improved CPT Class	42.1			
Worsened CPT Class	0			
No Change CPT Class	57.9			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With a Decrease, No Change, or Increase in Model for End Stage Liver Disease (MELD) Score

End point title	Percentage of Participants With a Decrease, No Change, or Increase in Model for End Stage Liver Disease (MELD) Score

End point description:

MELD score is a chronic liver disease severity scoring system. Scores can range from 6 to 40, with higher scores
indicating greater disease severity. "No change" was assigned for differences (posttreatment visits minus baseline
score) of -1, 0 or 1; "Decrease" was assigned for differences that were less than or equal to -2; and

"Increase" was
assigned for values that were greater than or equal to 2. Participants in the Full Analysis Set who achieved SVR24 with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline to Posttreatment Week 24

End point values	SOF/VEL+ RBV (Total)			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: Percentage of participants				
number (not applicable)				
Decrease (Improvement)	52.6			
No Change	21.1			
Increase (Worsening)	26.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute HCV RNA Level through Week 12

End point title	Absolute HCV RNA Level through Week 12

End point description:

Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Weeks 2, 4, 8, and 12

End point values	SOF/VEL+ RBV (Total)	SOF/VEL+ RBV (GT-1)	SOF/VEL+ RBV (GT-2)	SOF/VEL+ RBV (GT-3)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	32	18	5	7
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Baseline (N= 32, 18, 5, 7)	5.17 (± 1.187)	5.46 (± 0.537)	6.01 (± 0.502)	4.84 (± 1.058)
Week 2 (N =29, 16, 4, 7)	1.46 (± 0.392)	1.47 (± 0.387)	1.63 (± 0.150)	1.43 (± 0.526)
Week 4 (N = 28, 16, 3, 7)	1.15 (± 0.000)	1.15 (± 0.000)	1.15 (± 0.000)	1.15 (± 0.000)
Week 8 (N = 29, 16, 4, 7)	1.15 (± 0.000)	1.15 (± 0.000)	1.15 (± 0.000)	1.15 (± 0.000)
Week 12 (N = 29, 16, 4, 7)	1.15 (± 0.000)	1.15 (± 0.000)	1.15 (± 0.000)	1.15 (± 0.000)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in HCV RNA

End point title	Change From Baseline in HCV RNA

End point description:

Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Weeks 2, 4, 8, and 12

End point values	SOF/VEL+ RBV (Total)	SOF/VEL+ RBV (GT-1)	SOF/VEL+ RBV (GT-2)	SOF/VEL+ RBV (GT-3)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	29	16	4	7
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Change at Week 2 (N = 29, 16, 4, 7)	-3.72 (± 1.092)	-4.06 (± 0.531)	-4.50 (± 0.366)	-3.41 (± 0.665)
Change at Week 4 (N = 28, 16, 3, 7)	-3.99 (± 1.238)	-4.39 (± 0.520)	-4.88 (± 0.395)	-3.70 (± 1.058)
Change at Week 8 (N = 29, 16, 4, 7)	-4.00 (± 1.217)	-4.39 (± 0.520)	-4.72 (± 0.445)	-3.70 (± 1.058)
Change at Week 12 (N = 29, 16, 4, 7)	-4.00 (± 1.217)	-4.39 (± 0.520)	-4.72 (± 0.445)	-3.70 (± 1.058)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Virologic Failure

End point title	Number of Participants With Virologic Failure

End point description:

Virologic failure was defined as: - On-treatment virologic
failure: -- Breakthrough (confirmed HCV RNA ≥ LLOQ after having previously had HCV RNA < LLOQ while on
treatment), or -- Rebound (confirmed > 1 log10 IU/mL increase in HCV RNA from nadir while on treatment),
or -- Non-response (HCV RNA persistently ≥ LLOQ through 8 weeks of treatment) - Virologic relapse: -- Confirmed HCV RNA ≥ LLOQ during the posttreatment period having achieved HCV RNA < LLOQ at last on-treatment
visit. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Baseline to Posttreatment Week 12

End point values	SOF/VEL+ RBV (Total)	SOF/VEL+ RBV (GT-1)	SOF/VEL+ RBV (GT-2)	SOF/VEL+ RBV (GT-3)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	32	18	5	7
Units: participants				
number (not applicable)	1	0	0	1

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events: First dose date up to Week 12 plus 30 days; All-Cause Mortality: First dose date up to Posttreatment Week 24

Adverse event reporting additional description:

The Safety Analysis Set included all participants who took at least 1 dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	SOF/VEL+RBV

Reporting group description:

SOF/VEL (400/100 mg) FDC tablet once daily + RBV tablet (600-1200 mg based on weight) divided twice daily for 12 weeks in participants with HCV infection and Child-Pugh-Turcotte (CPT) Class C cirrhosis

Serious adverse events	SOF/VEL+RBV		
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 32 (53.13%)		
number of deaths (all causes)	8		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatocellular carcinoma			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Mixed hepatocellular cholangiocarcinoma			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ventricular tachycardia			

subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Hepatic encephalopathy			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Hepatic hydrothorax			

subjects affected / exposed	2 / 32 (6.25%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory distress				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Renal and urinary disorders				
Acute kidney injury				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Sepsis				
subjects affected / exposed	2 / 32 (6.25%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Dermo-hypodermitis				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia sepsis				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				

subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	SOF/VEL+RBV		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 32 (84.38%)		
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 32 (9.38%)		
occurrences (all)	3		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	8 / 32 (25.00%)		
occurrences (all)	9		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	6 / 32 (18.75%)		
occurrences (all)	6		
Fatigue			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Oedema peripheral			

subjects affected / exposed occurrences (all)	2 / 32 (6.25%) 2		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Ascites subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all)	 8 / 32 (25.00%) 8 5 / 32 (15.63%) 7 3 / 32 (9.38%) 3 3 / 32 (9.38%) 3 3 / 32 (9.38%) 3 2 / 32 (6.25%) 2		
Respiratory, thoracic and mediastinal disorders Hepatic hydrothorax subjects affected / exposed occurrences (all)	 2 / 32 (6.25%) 4		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	 2 / 32 (6.25%) 2		
Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all) Haematuria subjects affected / exposed occurrences (all)	 2 / 32 (6.25%) 6 2 / 32 (6.25%) 2		

Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	3 / 32 (9.38%)		
occurrences (all)	3		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Urinary tract infection			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 November 2016	• Added hepatitis B surface antibody (HBsAb) and hepatitis B core antibody (HBcAb) assessments to the screening procedures. HBcAb-positive subjects underwent additional hepatitis B virus (HBV) DNA measurements on Day 1; on-treatment Weeks 4, 8, and 12; and posttreatment Weeks 4, 12, and 24 to monitor for HBV reactivation • Added instructions for the upward and downward titration of RBV • Added an inclusion criterion that treatment-experienced individuals must have completed their most recent HCV treatment at least 8 weeks prior to screening • Added guidelines for the use of erythropoiesis-stimulating agents • Added an additional toxicity-based stopping criterion of alanine aminotransferase (ALT) ≥ 15 × upper limit of normal (ULN) • Added the formula for MELD and CPT score calculations

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported