Clinical trial results:
A Long Term Follow-up Registry of Subjects Who Did Not Achieve Sustained Virologic Response in Gilead-Sponsored Trials in Subjects with Chronic Hepatitis C Infection

Summary

EudraCT number	2011-000946-39
Trial protocol	DE GB FR CZ HU PL IT AT SE ES EE NL BE
Global end of trial date	09 April 2018

Results information

Result version number	v1 (current)
This version publication date	20 April 2019
First version publication date	20 April 2019

Trial information

Trial identification

Sponsor protocol code	GS-US-248-0123

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01457768
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	09 April 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 April 2018
Global end of trial reached?	Yes
Global end of trial date	09 April 2018
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 hepatitis C virus (HCV) viral sequences and the persistence or evolution of treatment-emergent viral mutations in participants who fail to achieve a sustained viral response (SVR) after treatment with a Gilead oral antiviral (OAV) containing regimen in a previous Gilead-sponsored hepatitis C study.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 December 2011
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	United States: 403
Country: Number of subjects enrolled	Australia: 38
Country: Number of subjects enrolled	Canada: 33
Country: Number of subjects enrolled	Puerto Rico: 16
Country: Number of subjects enrolled	New Zealand: 15
Country: Number of subjects enrolled	Netherlands: 3
Country: Number of subjects enrolled	Poland: 1
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	United Kingdom: 8
Country: Number of subjects enrolled	Czech Republic: 3
Country: Number of subjects enrolled	Estonia: 1
Country: Number of subjects enrolled	France: 11
Country: Number of subjects enrolled	Germany: 22
Country: Number of subjects enrolled	Italy: 2

Worldwide total number of subjects	567
EEA total number of subjects	62

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)	530
From 65 to 84 years	37
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in the United States, Australia, Canada, New Zealand, and Europe. The first participant was screened on 19 December 2011. The last study visit occurred on 09 April 2018.

Pre-assignment

Screening details:

570 participants consented to participate the study. Three participants who did not have at least 1 postenrollment visit were excluded from all analyses.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	SOF+RBV±PEG

Arm description:

Participants previously received sofosbuvir (SOF) + ribavirin (RBV) with or without pegylated interferon (PEG).

Arm type	Observational
Investigational medicinal product name	Sofosbuvir
Investigational medicinal product code	
Other name	SOF, Sovaldi®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

No treatment was administered in this observational study. Participants received SOF in a previous Gilead-sponsored study.

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

Dosage and administration details:

No treatment was administered in this observational study. Participants received RBV in a previous Gilead-sponsored study.

Investigational medicinal product name	Pegylated interferon
Investigational medicinal product code	
Other name	PEG
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

No treatment was administered in this observational study. Participants received PEG in a previous Gilead-sponsored study.

Arm title	LDV/SOF±RBV

Arm description:

Participants previously received ledipasvir/sofosbuvir (LDV/SOF) with or without RBV.

Arm type	Observational

Investigational medicinal product name	Ledipasvir/sofosbuvir
Investigational medicinal product code	
Other name	LDV/SOF, Harvoni®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

No treatment was administered in this observational study. Participants received LDV/SOF in a previous Gilead-sponsored study.

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

Dosage and administration details:

No treatment was administered in this observational study. Participants received RBV in a previous Gilead-sponsored study.

Arm title	SOF/VEL±RBV

Arm description:

Participants previously received sofosbuvir/velpatasvir (SOF/VEL) with or without RBV.

Arm type	Observational
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:

No treatment was administered in this observational study. Participants received SOF/VEL in a previous Gilead-sponsored study.

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

Dosage and administration details:

No treatment was administered in this observational study. Participants received RBV in a previous Gilead-sponsored study.

Arm title	SOF/VEL/VOX

Arm description:

Participants previously received sofosbuvir/velpatasvir/voxilaprevir (SOF/VEL/VOX).

Arm type	Observational
Investigational medicinal product name	Sofosbuvir/velpatasvir/voxilaprevir
Investigational medicinal product code	
Other name	SOF/VEL/VOX, Vosevi®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

No treatment was administered in this observational study. Participants received SOF/VEL/VOX in a previous Gilead-sponsored study.

Arm title	Other

Arm description:

Participants previously received other HCV treatment. Other HCV treatment included SOF and products other than those in above arms.

Arm type	Observational

No investigational medicinal product assigned in this arm

Number of subjects in period 1	SOF+RBV±PEG	LDV/SOF±RBV	SOF/VEL±RBV
Started	254	34	52
Completed	29	1	2
Not completed	225	33	50
Subject withdrew consent	14	4	4
Signed consent but did not meet eligibility	2	-	-
Death	2	1	1
Study discontinued	2	-	-
Investigator decision	1	-	-
Started anti-viral therapy for HCV	183	23	44
Lost to follow-up	21	5	1

Number of subjects in period 1	SOF/VEL/VOX	Other
Started	22	205
Completed	0	56
Not completed	22	149
Subject withdrew consent	2	21
Signed consent but did not meet eligibility	-	-
Death	-	1
Study discontinued	-	3
Investigator decision	2	1
Started anti-viral therapy for HCV	17	103
Lost to follow-up	1	20

Baseline characteristics

Reporting groups	
Reporting group title	SOF+RBV±PEG
Reporting group description:	
Participants previously received sofosbuvir (SOF) + ribavirin (RBV) with or without pegylated interferon (PEG).	
Reporting group title	LDV/SOF±RBV
Reporting group description:	
Participants previously received ledipasvir/sofosbuvir (LDV/SOF) with or without RBV.	
Reporting group title	SOF/VEL±RBV
Reporting group description:	
Participants previously received sofosbuvir/velpatasvir (SOF/VEL) with or without RBV.	
Reporting group title	SOF/VEL/VOX
Reporting group description:	
Participants previously received sofosbuvir/velpatasvir/voxilaprevir (SOF/VEL/VOX).	
Reporting group title	Other
Reporting group description:	
Participants previously received other HCV treatment. Other HCV treatment included SOF and products other than those in above arms.	

Reporting group values	SOF+RBV±PEG	LDV/SOF±RBV	SOF/VEL±RBV
Number of subjects	254	34	52
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	52	59	57
standard deviation	± 8.5	± 6.7	± 6.1
Gender categorical Units: Subjects			
Female	45	1	9
Male	209	33	43
Race Units: Subjects			
Black or African American	26	9	5
White	213	24	46
Asian	6	0	0
American Indian or Alaska Native	5	0	0
Native Hawaiian or Pacific Islander	2	1	0
Other	2	0	1
Not Disclosed	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	33	2	7
Not Hispanic or Latino	220	32	45
Not Reported	1	0	0

Reporting group values	SOF/VEL/VOX	Other	Total
Number of subjects	22	205	567
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	58	55	
standard deviation	± 7.1	± 7.2	-
Gender categorical Units: Subjects			
Female	5	65	125
Male	17	140	442
Race Units: Subjects			
Black or African American	3	30	73
White	18	171	472
Asian	0	4	10
American Indian or Alaska Native	0	0	5
Native Hawaiian or Pacific Islander	0	0	3
Other	1	0	4
Not Disclosed	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	2	21	65
Not Hispanic or Latino	20	182	499
Not Reported	0	2	3

End points

End points reporting groups

Reporting group title	SOF+RBV±PEG
Reporting group description:	
Participants previously received sofosbuvir (SOF) + ribavirin (RBV) with or without pegylated interferon (PEG).	
Reporting group title	LDV/SOF±RBV
Reporting group description:	
Participants previously received ledipasvir/sofosbuvir (LDV/SOF) with or without RBV.	
Reporting group title	SOF/VEL±RBV
Reporting group description:	
Participants previously received sofosbuvir/velpatasvir (SOF/VEL) with or without RBV.	
Reporting group title	SOF/VEL/VOX
Reporting group description:	
Participants previously received sofosbuvir/velpatasvir/voxilaprevir (SOF/VEL/VOX).	
Reporting group title	Other
Reporting group description:	
Participants previously received other HCV treatment. Other HCV treatment included SOF and products other than those in above arms.	
Subject analysis set title	SOF+RBV±PEG: Cirrhotic Participants
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants who previously received SOF+RBV±PEG and had cirrhosis at the parent study baseline were included in this analysis set.	
Subject analysis set title	LDV/SOF±RBV: Cirrhotic Participants
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants who previously received LDV/SOF±RBV and had cirrhosis at the parent study baseline were included in this analysis set.	
Subject analysis set title	SOF/VEL±RBV: Cirrhotic Participants
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants who previously received SOF/VEL±RBV and had cirrhosis at the parent study baseline were included in this analysis set.	
Subject analysis set title	SOF/VEL/VOX: Cirrhotic Participants
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants who previously received SOF/VEL/VOX and had cirrhosis at the parent study baseline were included in this analysis set.	
Subject analysis set title	Other: Cirrhotic Participants
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants who previously received other HCV treatment and had cirrhosis at the parent study baseline were included in this analysis set.	
Subject analysis set title	All Cirrhotic Participants
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants who had cirrhosis at the parent study baseline were included in this analysis set.	
Subject analysis set title	SOF+RBV±PEG: Non-Cirrhotic Participants
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants who previously received SOF+RBV±PEG and did not have cirrhosis (including participants	

with unknown cirrhosis status) at the parent study baseline were included in this analysis set.

Subject analysis set title	LDV/SOF±RBV: Non-Cirrhotic Participants
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who previously received LDV/SOF±RBV and did not have cirrhosis (including participants with unknown cirrhosis status) at the parent study baseline were included in this analysis set.

Subject analysis set title	SOF/VEL±RBV: Non-Cirrhotic Participants
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who previously received SOF/VEL±RBV and did not have cirrhosis (including participants with unknown cirrhosis status) at the parent study baseline were included in this analysis set.

Subject analysis set title	SOF/VEL/VOX: Non-Cirrhotic Participants
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who previously received SOF/VEL/VOX and did not have cirrhosis (including participants with unknown cirrhosis status) at the parent study baseline were included in this analysis set.

Subject analysis set title	Other: Non-Cirrhotic Participants
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who previously received other HCV treatment and did not have cirrhosis (including participants with unknown cirrhosis status) at the parent study baseline were included in this analysis set.

Subject analysis set title	All Non-Cirrhotic Participants
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who did not have cirrhosis (including participants with unknown cirrhosis status) at the parent study baseline were included in this analysis set.

Primary: Percentage of Participants With at Least 1 Resistance-Associated Variant (RAV) Loss

End point title	Percentage of Participants With at Least 1 Resistance-Associated Variant (RAV) Loss[1]

End point description:

The RAV count was defined as the count of any RAV that was not detected at baseline of the parent study for a participant, but was detected in any other visit. The total RAV count was defined as the sum of the RAV counts across all 3 HCV genes (NS5A, NS5B, and NS3) for a visit. The cumulative RAV count was defined as the union of the RAV counts across all visits from relapse for an HCV gene. The total cumulative RAV count was defined as the sum of the cumulative RAV counts across all 3 HCV genes. RAV loss was defined as the cumulative RAV count minus the last RAV count with value of ≥ 0. Participants in the Virological Analysis Set (participants with virology data from time of failure in the most recent treatment protocol [including participants with attempted sequencing but failed, and participants who are indicated as with no data available at a specific time point]) with total cumulative RAV count ≥ 1 and RAV count ≥ 0 in at least 1 of the HCV genes were included in the analysis.

End point type	Primary

End point timeframe:

Enrollment to End of Study (up to 3 years)

Notes:

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

End point values	SOF+RBV±PEG	LDV/SOF±RBV	SOF/VEL±RBV	SOF/VEL/VOX
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	18	23	2
Units: Percentage of Participants				
number (not applicable)	70.0	22.2	30.4	50.0

End point values	Other			
Subject group type	Reporting group			
Number of subjects analysed	165			
Units: Percentage of Participants				
number (not applicable)	75.2			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with RAV Loss by Unit Category

End point title	Percentage of Participants with RAV Loss by Unit Category

End point description:

RAV loss was defined as the cumulative RAV count minus the last RAV count with value of equal to or greater than 0. Percentage of participants with at least X RAV loss = (number of participants with at least X RAV loss divided by the number of participants with cumulative RAV count ≥ X) multiplied by 100. Participants in the Virological Analysis Set with total cumulative RAV count ≥ 1 and RAV count ≥ 0 in at least 1 of the HCV genes and with available data were analyzed. The value 99999 signifies that no participants were evaluable in the specified unit category, for indicated arm.

End point type	Secondary

End point timeframe:

Enrollment to End of Study (up to 3 years)

End point values	SOF+RBV±PEG	LDV/SOF±RBV	SOF/VEL±RBV	SOF/VEL/VOX
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	18	23	2
Units: Percentage of Participants				
number (not applicable)				
1 RAV Loss (n = 10, 18, 23, 2, 165)	70.0	22.2	30.4	50.0
2 RAV Loss (n = 0, 8, 5, 1, 151)	99999	25.0	20.0	0.0
3 RAV Loss (n = 0, 3, 0, 0, 114)	99999	0.0	99999	99999
4 RAV Loss (n = 0, 1, 0, 0, 97)	99999	0.0	99999	99999
5 RAV Loss (n = 0, 0, 0, 0, 65)	99999	99999	99999	99999
6 RAV Loss (n = 0, 0, 0, 0, 36)	99999	99999	99999	99999
7 RAV Loss (n = 0, 0, 0, 0, 21)	99999	99999	99999	99999
8 RAV Loss (n = 0, 0, 0, 0, 9)	99999	99999	99999	99999
9 RAV Loss (n = 0, 0, 0, 0, 7)	99999	99999	99999	99999
10 RAV Loss (n = 0, 0, 0, 0, 4)	99999	99999	99999	99999

End point values	Other			
Subject group type	Reporting group			
Number of subjects analysed	165			
Units: Percentage of Participants				
number (not applicable)				
1 RAV Loss (n = 10, 18, 23, 2, 165)	75.2			
2 RAV Loss (n = 0, 8, 5, 1, 151)	64.9			
3 RAV Loss (n = 0, 3, 0, 0, 114)	58.8			
4 RAV Loss (n = 0, 1, 0, 0, 97)	44.3			
5 RAV Loss (n = 0, 0, 0, 0, 65)	29.2			
6 RAV Loss (n = 0, 0, 0, 0, 36)	33.3			
7 RAV Loss (n = 0, 0, 0, 0, 21)	42.9			
8 RAV Loss (n = 0, 0, 0, 0, 9)	44.4			
9 RAV Loss (n = 0, 0, 0, 0, 7)	14.3			
10 RAV Loss (n = 0, 0, 0, 0, 4)	25.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Average Number of RAV Loss

End point title	Average Number of RAV Loss

End point description:

RAV loss was defined as the cumulative RAV count minus the last RAV count with value of ≥ 0. Average number of RAV loss = total number of RAV loss divided by number of participants with total cumulative RAV count ≥ 1 and RAV count ≥ 0 in at least 1 of the HCV genes. Participants in the Virological Analysis Set with total cumulative RAV count ≥ 1 and RAV count ≥ 0 in at least 1 of the HCV genes were analyzed.

End point type	Secondary

End point timeframe:

Enrollment to End of Study (up to 3 years)

End point values	SOF+RBV±PEG	LDV/SOF±RBV	SOF/VEL±RBV	SOF/VEL/VOX
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	18	23	2
Units: RAV loss				
number (not applicable)	0.7	0.3	0.3	0.5

End point values	Other			

Subject group type	Reporting group			
Number of subjects analysed	165			
Units: RAV loss				
number (not applicable)	2.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Liver Disease Progression, as Assessed by Percentage of Participants Experiencing Jaundice

End point title	Liver Disease Progression, as Assessed by Percentage of Participants Experiencing Jaundice

End point description:

Participants in the Full Analysis Set (all participants with at least 1 post-enrollment visit who have previously participated in a Gilead-sponsored HCV study, received at least 1 Gilead OAV and failed to achieve SVR, as defined in the original treatment protocol) with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Weeks 12, 24, 36, 48, 96, and 144

End point values	All Cirrhotic Participants	All Non-Cirrhotic Participants		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	140	427		
Units: Percentage of Participants				
number (not applicable)				
Baseline (n = 139, 422)	3.6	0.0		
Week 12 (n = 108, 363)	0.0	0.0		
Week 24 (n = 102, 338)	2.9	0.0		
Week 36 (n = 71, 275)	0.0	0.0		
Week 48 (n = 55, 233)	0.0	0.0		
Week 96 (n = 17, 154)	5.9	0.0		
Week 144 (n = 10, 90)	0.0	0.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Liver Disease Progression, as Assessed by Percentage of Participants Experiencing Ascites

End point title	Liver Disease Progression, as Assessed by Percentage of Participants Experiencing Ascites

End point description:

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

End point type	Secondary
End point timeframe: Baseline, Weeks 12, 24, 36, 48, 96, and 144	

End point values	All Cirrhotic Participants	All Non-Cirrhotic Participants		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	140	427		
Units: Percentage of Participants				
number (not applicable)				
Baseline (n = 139, 422)	5.8	0.0		
Week 12 (n = 108, 363)	6.5	0.0		
Week 24 (n = 102, 338)	4.9	0.0		
Week 36 (n = 71, 275)	2.8	0.0		
Week 48 (n = 55, 233)	5.5	0.4		
Week 96 (n = 17, 154)	11.8	0.6		
Week 144 (n = 10, 90)	0.0	0.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Liver Disease Progression, as Assessed by Percentage of Participants Experiencing Hepatic Encephalopathy

End point title	Liver Disease Progression, as Assessed by Percentage of Participants Experiencing Hepatic Encephalopathy
End point description: Participants in the Full Analysis Set with available data were analyzed.	
End point type	Secondary
End point timeframe: Baseline, Weeks 12, 24, 36, 48, 96, and 144	

End point values	All Cirrhotic Participants	All Non-Cirrhotic Participants		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	140	427		
Units: Percentage of Participants				
number (not applicable)				
Baseline (n = 139, 422)	4.3	0.7		
Week 12 (n = 108, 363)	5.6	0.0		
Week 24 (n = 102, 338)	5.9	0.0		
Week 36 (n = 71, 275)	4.2	0.0		
Week 48 (n = 55, 233)	7.3	0.4		

Week 96 (n = 17, 154)	11.8	0.0		
Week 144 (n = 10, 90)	10.0	0.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Liver Disease Progression, as Assessed by Percentage of Participants Experiencing Varices

End point title	Liver Disease Progression, as Assessed by Percentage of Participants Experiencing Varices
End point description:	
Participants in the Full Analysis Set with available data were analyzed.	
End point type	Secondary
End point timeframe:	
Baseline, Weeks 12, 24, 36, 48, 96, and 144	

End point values	All Cirrhotic Participants	All Non-Cirrhotic Participants		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	140	427		
Units: Percentage of Participants				
number (not applicable)				
Baseline (n = 139, 422)	11.5	0.0		
Week 12 (n = 108, 363)	5.6	0.0		
Week 24 (n = 102, 338)	3.9	0.0		
Week 36 (n = 71, 275)	4.2	0.4		
Week 48 (n = 55, 233)	10.9	0.0		
Week 96 (n = 17, 154)	11.8	1.3		
Week 144 (n = 10, 90)	10.0	0.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Liver Disease Progression, as Assessed by Percentage of Participants Experiencing Other Events Related to Liver Disease Progression Such as Transplantation

End point title	Liver Disease Progression, as Assessed by Percentage of Participants Experiencing Other Events Related to Liver Disease Progression Such as Transplantation
End point description:	
Participants in the Full Analysis Set with available data were analyzed.	
End point type	Secondary

End point timeframe:

Baseline, Weeks 12, 24, 36, 48, 96, and 144

End point values	All Cirrhotic Participants	All Non-Cirrhotic Participants		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	140	427		
Units: Percentage of Participants				
number (not applicable)				
Baseline (n = 139, 422)	0.0	0.5		
Week 12 (n = 108, 363)	0.0	0.3		
Week 24 (n = 102, 338)	0.0	0.3		
Week 36 (n = 71, 275)	0.0	0.4		
Week 48 (n = 55, 233)	1.8	0.0		
Week 96 (n = 17, 154)	0.0	0.0		
Week 144 (n = 10, 90)	0.0	0.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Liver Disease Progression, as Assessed by Percentage of Participants Experiencing Clinically Meaningful Changes from Registry Baseline in Any Laboratory Parameters

End point title	Liver Disease Progression, as Assessed by Percentage of Participants Experiencing Clinically Meaningful Changes from Registry Baseline in Any Laboratory Parameters

End point description:

Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Enrollment to End of Study (up to 3 years)

End point values	All Cirrhotic Participants	All Non-Cirrhotic Participants		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	140	427		
Units: Percentage of Participants				
number (not applicable)	0.0	0.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Developed Hepatocellular Carcinoma (HCC) Through Week 144

End point title	Percentage of Participants who Developed Hepatocellular Carcinoma (HCC) Through Week 144

End point description:

Percentage of participants who developed HCC was estimated by Kaplan-Meier estimate of the proportion of participants with HCC event by the time point. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Weeks 12, 24, 36, 48, 96, and 144

End point values	SOF+RBV±PEG: Cirrhotic Participants	LDV/SOF±RBV: Cirrhotic Participants	SOF/VEL±RBV: Cirrhotic Participants	SOF/VEL/VOX: Cirrhotic Participants
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	79	18	29	11
Units: Percentage of Participants				
number (not applicable)				
Baseline	0.00	0.00	0.00	0.00
Week 12	2.53	5.56	0.00	0.00
Week 24	3.92	5.56	0.00	0.00
Week 36	3.92	5.56	0.00	0.00
Week 48	3.92	5.56	0.00	0.00
Week 96	9.58	5.56	0.00	0.00
Week 144	27.7	5.56	0.00	0.00

End point values	Other: Cirrhotic Participants	All Cirrhotic Participants	SOF+RBV±PEG: Non-Cirrhotic Participants	LDV/SOF±RBV: Non-Cirrhotic Participants
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	140	175	16
Units: Percentage of Participants				
number (not applicable)				
Baseline	0.00	0.00	0.00	0.00
Week 12	0.00	2.14	0.00	0.00
Week 24	0.00	2.98	0.67	0.00
Week 36	0.00	2.98	0.67	0.00
Week 48	0.00	2.98	0.67	0.00
Week 96	0.00	6.71	0.67	0.00
Week 144	0.00	20.0	3.28	0.00

End point values	SOF/VEL±RBV: Non-Cirrhotic	SOF/VEL/VOX: Non-Cirrhotic	Other: Non-Cirrhotic	All Non-Cirrhotic

	Participants	Participants	Participants	Participants
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	23	11	202	427
Units: Percentage of Participants				
number (not applicable)				
Baseline	0.00	0.00	0.00	0.00
Week 12	0.00	0.00	0.00	0.00
Week 24	0.00	0.00	0.00	0.27
Week 36	0.00	0.00	0.00	0.27
Week 48	0.00	0.00	0.00	0.27
Week 96	0.00	0.00	0.00	0.27
Week 144	0.00	0.00	0.00	0.98

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Participants were not provided study drug in this registry study. There were no treatment-emergent adverse events (AEs) or serious adverse events (SAEs).

Adverse event reporting additional description:

Safety Analysis Set included all participants with at least 1 post-enrollment visit who have previously participated in a Gilead-sponsored HCV study, received at least 1 Gilead OAV and failed to achieve SVR, as defined in the original treatment protocol.

Assessment type	Systematic

Dictionary used

Dictionary name	No Dictionary
Dictionary version	0.0

Reporting groups

Reporting group title	SOF+RBV±PEG

Reporting group description:

Participants previously received sofosbuvir (SOF) + ribavirin (RBV) with or without pegylated interferon (PEG).

Reporting group title	LDV/SOF±RBV

Reporting group description:

Participants previously received ledipasvir/sofosbuvir (LDV/SOF) with or without RBV.

Reporting group title	SOF/VEL±RBV

Reporting group description:

Participants previously received sofosbuvir/velpatasvir (SOF/VEL) with or without RBV.

Reporting group title	SOF/VEL/VOX

Reporting group description:

Participants previously received sofosbuvir/velpatasvir/voxilaprevir (SOF/VEL/VOX).

Reporting group title	Other

Reporting group description:

Participants previously received other HCV treatment. Other HCV treatment included SOF and products other than those in above arms.

Serious adverse events	SOF+RBV±PEG	LDV/SOF±RBV	SOF/VEL±RBV
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 254 (0.00%)	0 / 34 (0.00%)	0 / 52 (0.00%)
number of deaths (all causes)	2	1	1
number of deaths resulting from adverse events	0	0	0

Serious adverse events	SOF/VEL/VOX	Other	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 22 (0.00%)	0 / 205 (0.00%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	SOF+RBV±PEG	LDV/SOF±RBV	SOF/VEL±RBV
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 254 (0.00%)	0 / 34 (0.00%)	0 / 52 (0.00%)

Non-serious adverse events	SOF/VEL/VOX	Other	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 22 (0.00%)	0 / 205 (0.00%)	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Participants were not provided study drug in this registry study. There were no treatment-emergent adverse events (AEs) or serious adverse events (SAEs).

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 June 2012	In this amendment, a quality of life survey was added to all study visits in Study GS-US-248-0123. Also, it was clarified that the detection of a drug resistant mutation (DRM) is no longer an inclusion criterion and the absence of a DRM is no longer a discontinuation criterion.
02 December 2014	The purpose of this amendment was to provide clarification to the protocol text that individual participants may be discontinued at the sponsor's discretion.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported