



Clinical trial results:

A Registry for Subjects With Cirrhosis Who Achieve a Sustained Virologic Response Following Treatment With a Sofosbuvir- Based Regimen Without Interferon for Chronic Hepatitis C Infection

Summary

EudraCT number	2014-001249-26
Trial protocol	DE ES GB IT
Global end of trial date	31 December 2021

Results information

Result version number	v1 (current)
This version publication date	21 December 2022
First version publication date	21 December 2022

Trial information

Trial identification

Sponsor protocol code	GS-US-337-1431
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02292706
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	31 December 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 December 2021
Global end of trial reached?	Yes
Global end of trial date	31 December 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this registry study was to assess the durability of sustained virologic response (SVR) and clinical progression or regression of liver disease including the incidence of hepatocellular carcinoma following SVR in participants with cirrhosis after treatment with a sofosbuvir-based regimen for Hepatitis C virus 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	29 December 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Regulatory reason
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 54
Country: Number of subjects enrolled	United Kingdom: 51
Country: Number of subjects enrolled	France: 122
Country: Number of subjects enrolled	Germany: 27
Country: Number of subjects enrolled	Italy: 26
Country: Number of subjects enrolled	United States: 1136
Country: Number of subjects enrolled	New Zealand: 70
Country: Number of subjects enrolled	Australia: 69
Country: Number of subjects enrolled	Canada: 54
Worldwide total number of subjects	1609
EEA total number of subjects	229

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)	1295
From 65 to 84 years	312
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Australia, Canada, France, Germany, Italy, New Zealand, Spain, the United Kingdom, and the United States.

Pre-assignment

Screening details:

1609 participants were enrolled in the registry. Of the 1609 enrolled participants, 1573 participants met eligibility criteria and were included in the analysis.

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

Arm description:

Participants who were previously treated with sofosbuvir (SOF) along with ribavirin (RBV) were followed up to 5 years.

Arm type	Observational
Investigational medicinal product name	Sofosbuvir
Investigational medicinal product code	
Other name	SOF, GS-7977, PSI-7977, Sovaldi®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

No treatment was administered in this study. Participants received SOF in a previous Gilead-sponsored study or at a subset of sites preselected by Gilead, who have previously received an all-oral SOF-based regimen outside a clinical 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 study. Participants received RBV in a previous Gilead-sponsored study or at a subset of sites preselected by Gilead, who have previously received an all-oral SOF-based regimen outside a clinical study.

Arm title	LDV/SOF
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Arm description:

Participants who were previously treated with ledipasvir (LDV)/SOF were followed up to 5 years.

Arm type	Observational
Investigational medicinal product name	Ledipasvir/sofosbuvir
Investigational medicinal product code	
Other name	LDV/SOF; Harvoni®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

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

sponsored study or at a subset of sites preselected by Gilead, who have previously received an all-oral SOF-based regimen outside a clinical study.

Arm title	LDV/SOF+RBV
Arm description:	
Participants who were previously treated with LDV/SOF along with RBV were followed up to 5 years.	
Arm type	Observational
Investigational medicinal product name	Ledipasvir/sofosbuvir
Investigational medicinal product code	
Other name	LDV/SOF; Harvoni®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

No treatment was administered in this study. Participants received LDV/SOF in a previous Gilead-sponsored study or at a subset of sites preselected by Gilead, who have previously received an all-oral SOF-based regimen outside a clinical 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 study. Participants received RBV in a previous Gilead-sponsored study or at a subset of sites preselected by Gilead, who have previously received an all-oral SOF-based regimen outside a clinical study.

Arm title	SOF/VEL
Arm description:	
Participants who were previously treated with SOF/velpatasvir (VEL) were followed up to 5 years.	
Arm type	Observational
Investigational medicinal product name	Sofosbuvir/velpatasvir
Investigational medicinal product code	
Other name	SOF/VEL; Epclusa®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

No treatment was administered in this study. Participants received SOF/VEL in a previous Gilead-sponsored study or at a subset of sites preselected by Gilead, who have previously received an all-oral SOF-based regimen outside a clinical study.

Arm title	SOF/VEL+RBV
Arm description:	
Participants who were previously treated with SOF/VEL along with RBV were followed up to 5 years.	
Arm type	Observational
Investigational medicinal product name	Sofosbuvir/velpatasvir
Investigational medicinal product code	
Other name	SOF/VEL; Epclusa®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

No treatment was administered in this study. Participants received SOF/VEL in a previous Gilead-sponsored study or at a subset of sites preselected by Gilead, who have previously received an all-oral SOF-based regimen outside a clinical 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 study. Participants received RBV in a previous Gilead-sponsored study or at a subset of sites preselected by Gilead, who have previously received an all-oral SOF-based regimen outside a clinical study.

Arm title	SOF/VEL/VOX
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Arm description:

Participants who were previously treated with SOF/VEL/voxilaprevir (VOX) with or without RBV were followed up to 5 years.

Arm type	Observational
Investigational medicinal product name	Sofosbuvir/velpatasvir/voxilaprevir
Investigational medicinal product code	
Other name	SOF/VEL/VOX; Vosevi®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

No treatment was administered in this study. Participants received SOF/VEL/VOX with or without RBV in a previous Gilead-sponsored study or at a subset of sites preselected by Gilead, who have previously received an all-oral SOF-based regimen outside a clinical study.

Arm title	Other SOF-Based
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Arm description:

Participants who previously received other SOF based regimen were followed up to 5 years. The other SOF-based regimens may have included the following BMS-790052 (Daclatasvir) + GS-7977 (SOF) with or without RBV, LDV/SOF + GS-9669, GS-7977 (SOF) + with or without RBV + TMC-435 (Simeprevir), LDV/SOF + Vedroprevir (VDV), LDV/SOF + GS-9669 (250 mg and 500 mg), LDV/SOF + VDV + RBV, Simeprevir+ SOF, and TMC-435 (Simeprevir) +VEL/SOF.

Arm type	Observational
Investigational medicinal product name	Sofosbuvir
Investigational medicinal product code	
Other name	SOF, GS-7977, PSI-7977, Sovaldi®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

No treatment was administered in this study. Participants received other SOF-based regimens in a previous Gilead-sponsored study or at a subset of sites preselected by Gilead, who have previously received an all-oral SOF-based regimen outside a clinical study.

Number of subjects in period 1^[1]	SOF+RBV	LDV/SOF	LDV/SOF+RBV
Started	94	275	263
Completed	49	145	157
Not completed	45	130	106
Virologic relapse or reinfection	1	-	-
Subject terminated by sponsor	1	-	-
Death	3	11	16
Liver transplant	1	1	11

Study terminated by sponsor	-	9	4
Lost to follow-up	20	44	24
Withdrew consent	15	56	43
Investigator's discretion	4	9	7
Missing	-	-	1

Number of subjects in period 1^[1]	SOF/VEL	SOF/VEL+RBV	SOF/VEL/VOX
Started	372	98	332
Completed	201	35	181
Not completed	171	63	151
Virologic relapse or reinfection	1	-	1
Subject terminated by sponsor	2	1	-
Death	22	8	17
Liver transplant	16	5	6
Study terminated by sponsor	21	11	13
Lost to follow-up	61	21	52
Withdrew consent	36	13	51
Investigator's discretion	11	4	10
Missing	1	-	1

Number of subjects in period 1^[1]	Other SOF-Based
Started	139
Completed	82
Not completed	57
Virologic relapse or reinfection	-
Subject terminated by sponsor	-
Death	3
Liver transplant	5
Study terminated by sponsor	3
Lost to follow-up	25
Withdrew consent	20
Investigator's discretion	1
Missing	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Thirty-six participants who were enrolled but did not meet the eligibility criteria were not included in the Safety Analysis Set reported in the above table.

Baseline characteristics

Reporting groups

Reporting group title	SOF+RBV
Reporting group description: Participants who were previously treated with sofosbuvir (SOF) along with ribavirin (RBV) were followed up to 5 years.	
Reporting group title	LDV/SOF
Reporting group description: Participants who were previously treated with ledipasvir (LDV)/SOF were followed up to 5 years.	
Reporting group title	LDV/SOF+RBV
Reporting group description: Participants who were previously treated with LDV/SOF along with RBV were followed up to 5 years.	
Reporting group title	SOF/VEL
Reporting group description: Participants who were previously treated with SOF/velpatasvir (VEL) were followed up to 5 years.	
Reporting group title	SOF/VEL+RBV
Reporting group description: Participants who were previously treated with SOF/VEL along with RBV were followed up to 5 years.	
Reporting group title	SOF/VEL/VOX
Reporting group description: Participants who were previously treated with SOF/VEL/voxilaprevir (VOX) with or without RBV were followed up to 5 years.	
Reporting group title	Other SOF-Based
Reporting group description: Participants who previously received other SOF based regimen were followed up to 5 years. The other SOF-based regimens may have included the following BMS-790052 (Daclatasvir) + GS-7977 (SOF) with or without RBV, LDV/SOF + GS-9669, GS-7977 (SOF) + with or without RBV + TMC-435 (Simeprevir), LDV/SOF + Velpatavir (VDV), LDV/SOF + GS-9669 (250 mg and 500 mg), LDV/SOF + VDV + RBV, Simeprevir+ SOF, and TMC-435 (Simeprevir) +VEL/SOF.	

Reporting group values	SOF+RBV	LDV/SOF	LDV/SOF+RBV
Number of subjects	94	275	263
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	56 ± 7.4	60 ± 7.8	60 ± 7.2
Gender categorical Units: Subjects			
Female	35	94	83
Male	59	181	180
Race Units: Subjects			
White	82	230	234
Black	3	40	19
Asian	7	3	4
American Indian or Alaska Native	1	0	2

Unknown or Not Reported	0	2	2
Native Hawaiian or Other Pacific Islander	1	0	1
Other	0	0	1
Ethnicity Units: Subjects			
Not Hispanic or Latino	87	239	219
Hispanic or Latino	7	34	41
Unknown or Not Reported	0	2	3

Reporting group values	SOF/VEL	SOF/VEL+RBV	SOF/VEL/VOX
Number of subjects	372	98	332
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	58	58	59
standard deviation	± 7.3	± 6.9	± 7.6
Gender categorical Units: Subjects			
Female	115	28	87
Male	257	70	245
Race Units: Subjects			
White	324	86	292
Black	25	5	26
Asian	17	5	8
American Indian or Alaska Native	4	0	1
Unknown or Not Reported	2	0	2
Native Hawaiian or Other Pacific Islander	0	1	2
Other	0	1	1
Ethnicity Units: Subjects			
Not Hispanic or Latino	331	90	281
Hispanic or Latino	35	8	49
Unknown or Not Reported	6	0	2

Reporting group values	Other SOF-Based	Total	
Number of subjects	139	1573	
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	59		
standard deviation	± 8.1	-	
Gender categorical Units: Subjects			
Female	55	497	

Male	84	1076	
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Race			
Units: Subjects			
White	117	1365	
Black	20	138	
Asian	0	44	
American Indian or Alaska Native	1	9	
Unknown or Not Reported	1	9	
Native Hawaiian or Other Pacific Islander	0	5	
Other	0	3	
Ethnicity			
Units: Subjects			
Not Hispanic or Latino	117	1364	
Hispanic or Latino	22	196	
Unknown or Not Reported	0	13	

End points

End points reporting groups

Reporting group title	SOF+RBV
Reporting group description: Participants who were previously treated with sofosbuvir (SOF) along with ribavirin (RBV) were followed up to 5 years.	
Reporting group title	LDV/SOF
Reporting group description: Participants who were previously treated with ledipasvir (LDV)/SOF were followed up to 5 years.	
Reporting group title	LDV/SOF+RBV
Reporting group description: Participants who were previously treated with LDV/SOF along with RBV were followed up to 5 years.	
Reporting group title	SOF/VEL
Reporting group description: Participants who were previously treated with SOF/velpatasvir (VEL) were followed up to 5 years.	
Reporting group title	SOF/VEL+RBV
Reporting group description: Participants who were previously treated with SOF/VEL along with RBV were followed up to 5 years.	
Reporting group title	SOF/VEL/VOX
Reporting group description: Participants who were previously treated with SOF/VEL/voxilaprevir (VOX) with or without RBV were followed up to 5 years.	
Reporting group title	Other SOF-Based
Reporting group description: Participants who previously received other SOF based regimen were followed up to 5 years. The other SOF-based regimens may have included the following BMS-790052 (Daclatasvir) + GS-7977 (SOF) with or without RBV, LDV/SOF + GS-9669, GS-7977 (SOF) + with or without RBV + TMC-435 (Simeprevir), LDV/SOF + Velpatasvir (VEL), LDV/SOF + GS-9669 (250 mg and 500 mg), LDV/SOF + VDV + RBV, Simeprevir+ SOF, and TMC-435 (Simeprevir) +VEL/SOF.	

Primary: Percentage of Participants Maintaining Sustained Virologic Response (SVR) at Week 240

End point title	Percentage of Participants Maintaining Sustained Virologic Response (SVR) at Week 240 ^[1]
End point description: SVR at Week 240 was defined as HCV RNA< lower limit of quantification (LLOQ i.e., 15 or 25 International Units Per Milliliter [IU/mL]) or last available HCV RNA< LLOQ with no subsequent follow-up values at Week 240 after enrollment in this registry study. Full Analysis Set included all participants who met all inclusion criteria and did not meet any of the exclusion criteria, and with at least one post-enrollment visit measurement available.	
End point type	Primary
End point timeframe: Week 240	
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: Percentage of participants who maintained SVR at Week 240 was estimated using a Kaplan-Meier model.	

End point values	SOF+RBV	LDV/SOF	LDV/SOF+RBV	SOF/VEL
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	94	275	263	372
Units: percentage of participants				
number (not applicable)	98.9	100	99.6	99.7

End point values	SOF/VEL+RBV	SOF/VEL/VOX	Other SOF-Based	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	98	332	139	
Units: percentage of participants				
number (not applicable)	100	99.6	100	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Any Liver-Associated Events

End point title	Percentage of Participants With Any Liver-Associated Events ^[2]
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End point description:

Participants in Full Analysis Set who did not develop liver-associated event prior to entering the registry study were analyzed.

End point type	Primary
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End point timeframe:

Enrollment up to 240 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: Percentages of participants with any liver-associated events since registry start (Enrollment) through Week 240 was estimated using a Kaplan Meier model.

End point values	SOF+RBV	LDV/SOF	LDV/SOF+RBV	SOF/VEL
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89	259	254	350
Units: percentage of participants				
number (not applicable)	18.7	15.0	24.8	18.1

End point values	SOF/VEL+RBV	SOF/VEL/VOX	Other SOF-Based	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	81	326	133	
Units: percentage of participants				
number (not applicable)	37.6	16.1	18.2	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Developed Hepatocellular Carcinoma (HCC) Through Week 240

End point title	Percentage of Participants Who Developed Hepatocellular Carcinoma (HCC) Through Week 240 ^[3]
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End point description:

Participants with de novo HCC since registry start were defined as participants who had not been identified with HCC prior to registry start and only had HCC since registry start. Participants in the Full Analysis Set with no HCC prior to this registry study were analyzed.

End point type	Primary
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End point timeframe:

Enrollment up to 240 weeks

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Percentage of participants who developed de novo HCC through Week 240 was estimated using a Kaplan-Meier model.

End point values	SOF+RBV	LDV/SOF	LDV/SOF+RBV	SOF/VEL
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	92	273	259	367
Units: percentage of participants				
number (not applicable)	11.8	5.01	10.8	10.8

End point values	SOF/VEL+RBV	SOF/VEL/VOX	Other SOF-Based	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	98	330	138	
Units: percentage of participants				
number (not applicable)	15.3	12.4	11.2	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Detectable HCV RNA Due to Re-emergence of Pre-existing Virus Through Week 240

End point title	Number of Participants With Detectable HCV RNA Due to Re-emergence of Pre-existing Virus Through Week 240
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End point description:

Participants in Full Analysis Set were analyzed.

End point type Secondary

End point timeframe:

Enrollment up to 240 weeks

End point values	SOF+RBV	LDV/SOF	LDV/SOF+RBV	SOF/VEL
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	94	275	263	372
Units: participants	0	0	0	0

End point values	SOF/VEL+RBV	SOF/VEL/VOX	Other SOF-Based	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	98	332	139	
Units: participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Detectable HCV Resistance Mutations Through Week 240

End point title Number of Participants With Detectable HCV Resistance Mutations Through Week 240

End point description:

Participants in Full Analysis Set were analyzed.

End point type Secondary

End point timeframe:

Enrollment up to 240 weeks

End point values	SOF+RBV	LDV/SOF	LDV/SOF+RBV	SOF/VEL
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	94	275	263	372
Units: participants	0	0	1	0

End point values	SOF/VEL+RBV	SOF/VEL/VOX	Other SOF-Based	
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Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	98	332	139	
Units: participants	0	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Detectable HCV RNA Due to Re-infection Through Week 240

End point title	Number of Participants With Detectable HCV RNA Due to Re-infection Through Week 240
End point description: Reinfection was defined as HCV RNA > LLOQ on 2 samples collected at least 1 week apart with a different virus than that present prior to treatment baseline in the parent study. Participants in Full Analysis Set were analyzed.	
End point type	Secondary
End point timeframe: Enrollment up to 240 weeks	

End point values	SOF+RBV	LDV/SOF	LDV/SOF+RBV	SOF/VEL
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	94	275	263	372
Units: participants	0	0	0	1

End point values	SOF/VEL+RBV	SOF/VEL/VOX	Other SOF-Based	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	98	332	139	
Units: participants	0	1	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-Cause Mortality and Adverse Events: From enrollment up to a maximum duration of 5 years

No study treatments were given to study participants; thus, reported adverse events refer to AEs related to study procedures.

Adverse event reporting additional description:

All-Cause Mortality: Included participants who signed informed consent and enrolled into study. No deaths among participants who were enrolled but did not meet eligibility criteria. AEs: Included all participants who met all inclusion criteria and did not meet any of exclusion criteria, and with at least one post-enrollment visit measurement available.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.1
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Reporting groups

Reporting group title	SOF+RBV
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Reporting group description:

Participants who were previously treated with SOF along with RBV were followed up to 5 years.

Reporting group title	LDV/SOF
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Reporting group description:

Participants who were previously treated with LDV/SOF were followed up to 5 years.

Reporting group title	LDV/SOF+RBV
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Reporting group description:

Participants who were previously treated with LDV/SOF along with RBV were followed up to 5 years.

Reporting group title	SOF/VEL
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Reporting group description:

Participants who were previously treated with SOF/VEL were followed up to 5 years.

Reporting group title	SOF/VEL+RBV
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Reporting group description:

Participants who were previously treated with SOF/VEL along with RBV were followed up to 5 years.

Reporting group title	SOF/VEL/VOX
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Reporting group description:

Participants who were previously treated with SOF/VEL/VOX with or without RBV were followed up to 5 years.

Reporting group title	Other SOF-Based
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Reporting group description:

Participants who previously received other SOF based regimen were followed up to 5 years.

Serious adverse events	SOF+RBV	LDV/SOF	LDV/SOF+RBV
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 94 (0.00%)	0 / 275 (0.00%)	0 / 263 (0.00%)
number of deaths (all causes)	3	11	16
number of deaths resulting from adverse events	0	0	0

Serious adverse events	SOF/VEL	SOF/VEL+RBV	SOF/VEL/VOX
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 372 (0.00%)	0 / 98 (0.00%)	0 / 332 (0.00%)
number of deaths (all causes)	22	8	17
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Other SOF-Based		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 139 (0.00%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	SOF+RBV	LDV/SOF	LDV/SOF+RBV
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 94 (0.00%)	4 / 275 (1.45%)	1 / 263 (0.38%)
Injury, poisoning and procedural complications			
Incision site rash			
subjects affected / exposed	0 / 94 (0.00%)	0 / 275 (0.00%)	0 / 263 (0.00%)
occurrences (all)	0	0	0
Post procedural complication			
subjects affected / exposed	0 / 94 (0.00%)	0 / 275 (0.00%)	1 / 263 (0.38%)
occurrences (all)	0	0	1
Procedural complication			
subjects affected / exposed	0 / 94 (0.00%)	1 / 275 (0.36%)	0 / 263 (0.00%)
occurrences (all)	0	1	0
Procedural dizziness			
subjects affected / exposed	0 / 94 (0.00%)	1 / 275 (0.36%)	0 / 263 (0.00%)
occurrences (all)	0	1	0
Procedural pain			
subjects affected / exposed	0 / 94 (0.00%)	0 / 275 (0.00%)	0 / 263 (0.00%)
occurrences (all)	0	0	0

Nervous system disorders			
Paraesthesia			
subjects affected / exposed	0 / 94 (0.00%)	0 / 275 (0.00%)	0 / 263 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 94 (0.00%)	0 / 275 (0.00%)	0 / 263 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Vessel puncture site haematoma			
subjects affected / exposed	0 / 94 (0.00%)	2 / 275 (0.73%)	0 / 263 (0.00%)
occurrences (all)	0	2	0

Non-serious adverse events	SOF/VEL	SOF/VEL+RBV	SOF/VEL/VOX
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 372 (0.27%)	0 / 98 (0.00%)	1 / 332 (0.30%)
Injury, poisoning and procedural complications			
Incision site rash			
subjects affected / exposed	0 / 372 (0.00%)	0 / 98 (0.00%)	1 / 332 (0.30%)
occurrences (all)	0	0	1
Post procedural complication			
subjects affected / exposed	0 / 372 (0.00%)	0 / 98 (0.00%)	0 / 332 (0.00%)
occurrences (all)	0	0	0
Procedural complication			
subjects affected / exposed	0 / 372 (0.00%)	0 / 98 (0.00%)	0 / 332 (0.00%)
occurrences (all)	0	0	0
Procedural dizziness			
subjects affected / exposed	0 / 372 (0.00%)	0 / 98 (0.00%)	0 / 332 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 372 (0.00%)	0 / 98 (0.00%)	1 / 332 (0.30%)
occurrences (all)	0	0	1
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	1 / 372 (0.27%)	0 / 98 (0.00%)	0 / 332 (0.00%)
occurrences (all)	1	0	0
Presyncope			

subjects affected / exposed occurrences (all)	1 / 372 (0.27%) 1	0 / 98 (0.00%) 0	0 / 332 (0.00%) 0
General disorders and administration site conditions Vessel puncture site haematoma subjects affected / exposed occurrences (all)	0 / 372 (0.00%) 0	0 / 98 (0.00%) 0	0 / 332 (0.00%) 0

Non-serious adverse events	Other SOF-Based		
Total subjects affected by non-serious adverse events subjects affected / exposed	1 / 139 (0.72%)		
Injury, poisoning and procedural complications Incision site rash subjects affected / exposed occurrences (all)	0 / 139 (0.00%) 0		
Post procedural complication subjects affected / exposed occurrences (all)	0 / 139 (0.00%) 0		
Procedural complication subjects affected / exposed occurrences (all)	0 / 139 (0.00%) 0		
Procedural dizziness subjects affected / exposed occurrences (all)	0 / 139 (0.00%) 0		
Procedural pain subjects affected / exposed occurrences (all)	0 / 139 (0.00%) 0		
Nervous system disorders Paraesthesia subjects affected / exposed occurrences (all)	0 / 139 (0.00%) 0		
Presyncope subjects affected / exposed occurrences (all)	0 / 139 (0.00%) 0		
General disorders and administration site conditions Vessel puncture site haematoma			

subjects affected / exposed	1 / 139 (0.72%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 October 2014	• The purpose of this amendment was to clarify clinical laboratory and liver disease assessments. In addition, language was added to clarify the study conduct and patient enrollment of the Cirrhosis SVR Registry Study • The Gilead Study Director and Medical Monitor were changed • Reference to a Baseline visit was removed throughout. This was officially known as Day 1 • Minor wording changes were made to correct grammar and for clarity • Typographical edits were incorporated to ensure consistency and for clarification as needed.
17 August 2015	The purpose of this Amendment was to expand the inclusion criteria to allow cirrhotic subjects successfully achieved SVR after having been treated with commercial all-oral SOF-based regimen to participate in this Registry Study at pre-selected Gilead sites. Relevant sections of the protocol were updated to reflect this change as detailed below. This amendment also increased the window from the date of the final visit in the Gilead sponsored treatment study to entry into this Registry Study (Day 1 Assessment) from 48 to 60 weeks for those subjects who were previously treated in a Gilead sponsored study. Subjects who were enrolled in this registry from the Gilead HCV development programs continued in this registry as appropriate.
01 June 2017	• An optional whole blood sample collection for genetic analysis was added at Day 1, Week 96, and the final study visit, i.e., Week 240 or Early Termination for subjects who consented • The Study Director/Medical Monitor information was updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/32707225>

<http://www.ncbi.nlm.nih.gov/pubmed/33493697>