Clinical trial results:
A Long Term Follow-up Registry for Subjects Who Achieve a Sustained Virologic Response to Treatment in Gilead Sponsored Trials in Subjects with Chronic Hepatitis C Infection

Summary

EudraCT number	2011-000945-19
Trial protocol	DE GB FR CZ HU PL IT AT SE ES EE NL BE
Global end of trial date	08 January 2018

Results information

Result version number	v1 (current)
This version publication date	03 January 2019
First version publication date	03 January 2019

Trial information

Trial identification

Sponsor protocol code	GS-US-248-0122

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01457755
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	08 January 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 January 2018
Global end of trial reached?	Yes
Global end of trial date	08 January 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the durability of sustained virologic response (SVR) following treatment in a 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	13 April 2012
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: 4287
Country: Number of subjects enrolled	France: 588
Country: Number of subjects enrolled	New Zealand: 331
Country: Number of subjects enrolled	Germany: 265
Country: Number of subjects enrolled	United Kingdom: 261
Country: Number of subjects enrolled	Australia: 250
Country: Number of subjects enrolled	Canada: 199
Country: Number of subjects enrolled	Italy: 172
Country: Number of subjects enrolled	Spain: 99
Country: Number of subjects enrolled	Poland: 46
Country: Number of subjects enrolled	Netherlands: 24
Country: Number of subjects enrolled	Sweden: 22
Country: Number of subjects enrolled	Belgium: 20
Country: Number of subjects enrolled	Czech Republic: 19
Country: Number of subjects enrolled	Austria: 11
Country: Number of subjects enrolled	Estonia: 8
Country: Number of subjects enrolled	Puerto Rico: 5

Worldwide total number of subjects	6607
EEA total number of subjects	1535

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)	5886
From 65 to 84 years	721
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled in North America, Europe, Australia, and New Zealand. The first participant was screened on 13 April 2012. The last study visit occurred on 08 January 2018.

Pre-assignment

Screening details:

6623 participants were screened.

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 sofosbuvir 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.

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	1724	2204	1422
Completed	1138	1278	302
Not completed	586	926	1120
Virologic Relapse	12	7	3
Study Discontinued	74	154	802
Subject Withdrew Consent	174	177	87
Enrolled into HCV SVR Cirrhosis Registry Study	62	273	83
Death	8	20	6
Investigator Decision	15	16	6
Lost to follow-up	241	279	133

Number of subjects in period 1	SOF/VEL/VOX	Other
Started	597	660
Completed	0	163
Not completed	597	497
Virologic Relapse	1	5
Study Discontinued	537	337
Subject Withdrew Consent	16	46
Enrolled into HCV SVR Cirrhosis Registry Study	7	30
Death	2	4
Investigator Decision	2	2
Lost to follow-up	32	73

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.	

Reporting group values	SOF+RBV±PEG	LDV/SOF±RBV	SOF/VEL±RBV
Number of subjects	1724	2204	1422
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	52	55	55
standard deviation	± 9.7	± 9.6	± 10.1
Gender categorical Units: Subjects			
Female	607	800	578
Male	1117	1404	844
Race Units: Subjects			
Black or African American	112	301	128
White	1489	1843	1194
Asian	71	25	69
American Indian or Alaska Native	13	6	12
Native Hawaiian or Pacific Islander	6	8	4
Other	26	16	14
Not Disclosed	7	5	1
Ethnicity Units: Subjects			
Hispanic or Latino	203	217	128
Not Hispanic or Latino	1508	1978	1292
Not Reported	12	9	2
Missing	1	0	0

Reporting group values	SOF/VEL/VOX	Other	Total
Number of subjects	597	660	6607
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	56	51	
standard deviation	± 10.2	± 10.9	-
Gender categorical Units: Subjects			
Female	233	287	2505
Male	364	373	4102
Race Units: Subjects			
Black or African American	73	51	665
White	486	562	5574
Asian	31	27	223
American Indian or Alaska Native	5	6	42
Native Hawaiian or Pacific Islander	0	2	20
Other	2	9	67
Not Disclosed	0	3	16
Ethnicity Units: Subjects			
Hispanic or Latino	52	69	669
Not Hispanic or Latino	545	586	5909
Not Reported	0	5	28
Missing	0	0	1

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.	

Primary: Percentage of Participants Maintaining Sustained Virologic Response (SVR) at Week 144

End point title	Percentage of Participants Maintaining Sustained Virologic Response (SVR) at Week 144[1]
End point description:	
Participants in the Full Analysis Set (all participants with at least one post-enrollment visit who have previously participated in a Gilead-sponsored HCV study, received at least 1 Gilead OAV and achieved SVR, as defined in the original treatment protocol) with available data were analyzed.	
End point type	Primary
End point timeframe:	
At Week 144	

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 in this observational study.

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	1721[2]	2204	1422	597
Units: Percentage of Participants				
number (not applicable)	98.8	99.6	99.7	99.8

Notes:

[2] - 3 out of 1724 participants had missing HCV RNA data

End point values	Other			
Subject group type	Reporting group			
Number of subjects analysed	659[3]			
Units: Percentage of Participants				
number (not applicable)	99.2			

Notes:
[3] - 1 out of 660 participants had missing HCV RNA data

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 one post-enrollment visit who have previously participated in a Gilead-sponsored HCV study, received at least 1 Gilead OAV and achieved SVR, as defined in the original treatment protocol.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

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.

Serious adverse events	SOF+RBV±PEG	LDV/SOF±RBV	SOF/VEL±RBV
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1724 (0.00%)	0 / 2204 (0.00%)	0 / 1422 (0.00%)
number of deaths (all causes)	8	20	6
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 / 597 (0.00%)	0 / 660 (0.00%)	
number of deaths (all causes)	2	4	
number of deaths resulting from adverse events	0	0	

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

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 / 1724 (0.00%)	0 / 2204 (0.00%)	0 / 1422 (0.00%)

Non-serious adverse events	SOF/VEL/VOX	Other	
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 597 (0.00%)	0 / 660 (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 AEs or SAEs.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 June 2012	A quality of life survey added to all study visits in GS-US-248-0122. The window for rolling a patient over from the treatment protocol increased from 60 days to 90 days for scheduling flexibility.
02 December 2014	The purpose of this Amendment was to revise the protocol text that individual participants may be discontinued at the Sponsor's discretion. The current protocol language implies that Gilead may only discontinue the entire Registry Study. This amendment clarifies that Gilead may discontinue individual participants in the Registry Study once regulatory requirements are met.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported