Clinical trial results:
A Phase 3b, Multicenter, Open-Label Study to Evaluate the Safety and Efficacy of Ledipasvir/Sofosbuvir in Adults with Chronic HCV Infection

Summary

EudraCT number	2015-000690-13
Trial protocol	EE
Global end of trial date	30 June 2016

Results information

Result version number	v1 (current)
This version publication date	25 May 2017
First version publication date	25 May 2017

Trial information

Trial identification

Sponsor protocol code	GS-US-337-1463

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02472886
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Clinical Trials Mailbox, Gilead Sciences International Ltd, ClinicalTrialDisclosures@gilead.com
Scientific contact	Clinical Trials Mailbox, Gilead Sciences International Ltd, ClinicalTrialDisclosures@gilead.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 June 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 June 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study are to evaluate the antiviral efficacy, safety, and tolerability of ledipasvir/sofosbuvir (LDV/SOF) fixed dose combination (FDC) with or without ribavirin (RBV) in adults with chronic hepatitis C virus (HCV) infection.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 June 2015
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	Estonia: 18
Country: Number of subjects enrolled	Russian Federation: 135
Worldwide total number of subjects	153
EEA total number of subjects	18

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)	149
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Russia and Estonia. The first participant was screened on 17 June 2015. The last study visit occurred on 30 June 2016.

Pre-assignment

Screening details:

169 participants were screened.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	LDV/SOF 8 Weeks (TN, HCV-monoinfected [Group 1])

Arm description:

Ledipasvir/sofosbuvir (LDV/SOF; Harvoni®) (90/400 mg) fixed dose combination (FDC) tablet once daily for 8 weeks in treatment-naive (TN) participants with genotype 1 HCV infection without cirrhosis

Arm type	Experimental
Investigational medicinal product name	Ledipasvir/sofosbuvir
Investigational medicinal product code	
Other name	LDV/SOF, GS-5885/GS-7977, Harvoni®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

90/400 mg FDC once daily for 8 weeks

Arm title	LDV/SOF 8 Weeks (TN, HCV/HIV-coinfected [Group 2])

Arm description:

LDV/SOF (90/400 mg) FDC tablet once daily for 8 weeks in treatment naïve participants with genotype 1 HCV infection without cirrhosis and coinfected with HIV-1

Arm type	Experimental
Investigational medicinal product name	Ledipasvir/sofosbuvir
Investigational medicinal product code	
Other name	LDV/SOF, GS-5885/GS-7977, Harvoni®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

90/400 mg FDC once daily for 8 weeks

Arm title	LDV/SOF+RBV 12 Wks (TE,SOF-treated,HCV-monoinfected [Group 3])

Arm description:

LDV/SOF (90/400 mg) FDC tablet once daily + weight-based ribavirin (RBV) (1000-1200 mg in a divided daily dose) for 12 weeks in treatment-experienced (TE) participants with genotype 1 or 3 HCV infection who failed to achieve sustained virologic response (SVR) in a previous Gilead sofosbuvir (SOF) study

Arm type	Experimental

Investigational medicinal product name	Ledipasvir/sofosbuvir
Investigational medicinal product code	
Other name	LDV/SOF, GS-5885/GS-7977, Harvoni®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

90/400 mg FDC once daily for 12 weeks

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

Dosage and administration details:

Weight based RBV (1000-1200 mg in a divided daily dose) for 12 weeks

Number of subjects in period 1	LDV/SOF 8 Weeks (TN, HCV-monoinfected [Group 1])	LDV/SOF 8 Weeks (TN, HCV/HIV-coinfected [Group 2])	LDV/SOF+RBV 12 Wks (TE,SOF-treated,HCV-monoinfected [Group 3])
Started	67	59	27
Completed	67	57	26
Not completed	0	2	1
Lack of efficacy	-	2	1

Baseline characteristics

Reporting groups	
Reporting group title	LDV/SOF 8 Weeks (TN, HCV-monoinfected [Group 1])
Reporting group description:	
Ledipasvir/sofosbuvir (LDV/SOF; Harvoni®) (90/400 mg) fixed dose combination (FDC) tablet once daily for 8 weeks in treatment-naive (TN) participants with genotype 1 HCV infection without cirrhosis	
Reporting group title	LDV/SOF 8 Weeks (TN, HCV/HIV-coinfected [Group 2])
Reporting group description:	
LDV/SOF (90/400 mg) FDC tablet once daily for 8 weeks in treatment naïve participants with genotype 1 HCV infection without cirrhosis and coinfected with HIV-1	
Reporting group title	LDV/SOF+RBV 12 Wks (TE,SOF-treated,HCV-monoinfected [Group 3])
Reporting group description:	
LDV/SOF (90/400 mg) FDC tablet once daily + weight-based ribavirin (RBV) (1000-1200 mg in a divided daily dose) for 12 weeks in treatment-experienced (TE) participants with genotype 1 or 3 HCV infection who failed to achieve sustained virologic response (SVR) in a previous Gilead sofosbuvir (SOF) study	

Reporting group values	LDV/SOF 8 Weeks (TN, HCV-monoinfected [Group 1])	LDV/SOF 8 Weeks (TN, HCV/HIV-coinfected [Group 2])	LDV/SOF+RBV 12 Wks (TE,SOF-treated,HCV-monoinfected [Group 3])
Number of subjects	67	59	27
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	42	34	47
standard deviation	± 12.6	± 5.5	± 11.2
Gender categorical Units: Subjects			
Female	33	25	9
Male	34	34	18
Race Units: Subjects			
White	66	59	27
Asian	1	0	0
Ethnicity Units: Subjects			
Not Hispanic or Latino	67	59	27
IL28b Status			
The CC, CT, and TT alleles are different forms of the IL28b gene.			
Units: Subjects			
CC	17	9	7
CT	41	41	18
TT	9	9	2
HCV RNA Category Units: Subjects			
< 800,000 IU/mL	29	23	8
≥ 800,000 IU/mL	38	36	19

Cirrhosis Status Units: Subjects			
No	67	59	17
Yes	0	0	10
HCV RNA Units: log10 IU/mL			
arithmetic mean	5.9	6.1	6.3
standard deviation	± 0.72	± 0.54	± 0.67

Reporting group values	Total		
Number of subjects	153		
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	67		
Male	86		
Race Units: Subjects			
White	152		
Asian	1		
Ethnicity Units: Subjects			
Not Hispanic or Latino	153		
IL28b Status			
The CC, CT, and TT alleles are different forms of the IL28b gene.			
Units: Subjects			
CC	33		
CT	100		
TT	20		
HCV RNA Category Units: Subjects			
< 800,000 IU/mL	60		
≥ 800,000 IU/mL	93		
Cirrhosis Status Units: Subjects			
No	143		
Yes	10		
HCV RNA Units: log10 IU/mL			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	LDV/SOF 8 Weeks (TN, HCV-monoinfected [Group 1])
Reporting group description:	
Ledipasvir/sofosbuvir (LDV/SOF; Harvoni®) (90/400 mg) fixed dose combination (FDC) tablet once daily for 8 weeks in treatment-naive (TN) participants with genotype 1 HCV infection without cirrhosis	
Reporting group title	LDV/SOF 8 Weeks (TN, HCV/HIV-coinfected [Group 2])
Reporting group description:	
LDV/SOF (90/400 mg) FDC tablet once daily for 8 weeks in treatment naïve participants with genotype 1 HCV infection without cirrhosis and coinfected with HIV-1	
Reporting group title	LDV/SOF+RBV 12 Wks (TE,SOF-treated,HCV-monoinfected [Group 3])
Reporting group description:	
LDV/SOF (90/400 mg) FDC tablet once daily + weight-based ribavirin (RBV) (1000-1200 mg in a divided daily dose) for 12 weeks in treatment-experienced (TE) participants with genotype 1 or 3 HCV infection who failed to achieve sustained virologic response (SVR) in a previous Gilead sofosbuvir (SOF) study	
Subject analysis set title	LDV/SOF 8 Weeks (TN, HCV/HIV-coinfected, ARV-Naive)
Subject analysis set type	Safety analysis
Subject analysis set description:	
LDV/SOF (90/400 mg) FDC tablet once daily for 8 weeks in treatment naive participants with genotype 1 HCV infection without cirrhosis and coinfected with HIV-1. These participants did not receive any prior ARV therapy. Participant in the Safety analysis set (without any prior ARV treatment) with available data were analyzed.	
Subject analysis set title	LDV/SOF 8 Weeks (TN, HCV/HIV-coinfected, ARV-Experienced)
Subject analysis set type	Safety analysis
Subject analysis set description:	
LDV/SOF (90/400 mg) FDC tablet once daily for 8 weeks in treatment-naive participants with genotype 1 HCV infection without cirrhosis and coinfected with HIV-1. These participants were on a stable ARV regimen for at least 8 weeks prior to screening. Participant in the Safety analysis set (who received prior ARV treatment) with available data were analyzed	

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

End point title	Percentage of Participants With Sustained Virologic Response 12 Weeks After Discontinuation of Therapy (SVR12)[1]
End point description:	
Full Analysis Set (FAS) included participants who were enrolled into the study and received 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	LDV/SOF 8 Weeks (TN, HCV-monoinfected [Group 1])	LDV/SOF 8 Weeks (TN, HCV/HIV-coinfected [Group 2])	LDV/SOF+RBV 12 Wks (TE,SOF-treated,HCV-monoinfected [Group 3])	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	67	59	27	
Units: percentage of participants				

number (confidence interval 95%)	100 (94.6 to 100)	96.6 (88.3 to 99.6)	96.3 (81 to 99.9)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Discontinued Study Drug Due to Any Adverse Event (AE)

End point title	Percentage of Participants Who Discontinued Study Drug Due to Any Adverse Event (AE)[2]

End point description:

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

End point type	Primary

End point timeframe:

Up to 12 weeks

Notes:

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

End point values	LDV/SOF 8 Weeks (TN, HCV-monoinfected [Group 1])	LDV/SOF 8 Weeks (TN, HCV/HIV-coinfected [Group 2])	LDV/SOF+RBV 12 Wks (TE,SOF-treated,HCV-monoinfected [Group 3])	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	67	59	27	
Units: percentage of participants				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Sustained Virologic Response (SVR) at 4 and 24 Weeks After Discontinuation of Therapy (SVR4 and SVR24)

End point title	Percentage of Participants With Sustained Virologic Response (SVR) at 4 and 24 Weeks After Discontinuation of Therapy (SVR4 and SVR24)

End point description:

SVR4 and SVR24 were defined as HCV RNA < LLOQ at 4 and 24 weeks following the last dose of study drug, respectively. Full Analysis Set

End point type	Secondary

End point timeframe:

Posttreatment Weeks 4 and 24

End point values	LDV/SOF 8 Weeks (TN, HCV-monoinfected [Group 1])	LDV/SOF 8 Weeks (TN, HCV/HIV-coinfected [Group 2])	LDV/SOF+RBV 12 Wks (TE,SOF-treated,HCV-monoinfected [Group 3])	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	67	59	27	
Units: percentage of participants				
number (confidence interval 95%)				
SVR4	100 (94.6 to 100)	96.6 (88.3 to 99.6)	96.3 (81 to 99.9)	
SVR24	100 (94.6 to 100)	96.6 (88.3 to 99.6)	96.3 (81 to 99.9)	

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Participants With HCV RNA < LLOQ on Treatment
End point description:	
1) Full Analysis Set 2) 999 = Treatment for this group was 8 weeks only.	
End point type	Secondary
End point timeframe:	
Up to 12 weeks	

End point values	LDV/SOF 8 Weeks (TN, HCV-monoinfected [Group 1])	LDV/SOF 8 Weeks (TN, HCV/HIV-coinfected [Group 2])	LDV/SOF+RBV 12 Wks (TE,SOF-treated,HCV-monoinfected [Group 3])	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	67	59	27	
Units: percentage of participants				
number (confidence interval 95%)				
Week 1	20.9 (11.9 to 32.6)	39 (26.5 to 52.6)	3.7 (0.1 to 19)	
Week 2	65.7 (53.1 to 76.8)	69.5 (56.1 to 80.8)	59.3 (38.8 to 77.6)	
Week 4	100 (94.6 to 100)	96.6 (88.3 to 99.6)	88.9 (70.8 to 97.6)	
Week 8	100 (94.6 to 100)	98.3 (90.9 to 100)	100 (87.2 to 100)	
Week 12	999 (999 to 999)	999 (999 to 999)	100 (87.2 to 100)	

Statistical analyses

No statistical analyses for this end point

Secondary: HCV RNA Change From Day 1

End point title	HCV RNA Change From Day 1

End point description:

1) Participants in Full Analysis Set with available data were analyzed. 2) 999 = Treatment for this group was 8 weeks only.

End point type	Secondary

End point timeframe:

Up to 12 weeks

End point values	LDV/SOF 8 Weeks (TN, HCV-monoinfected [Group 1])	LDV/SOF 8 Weeks (TN, HCV/HIV-coinfected [Group 2])	LDV/SOF+RBV 12 Wks (TE,SOF-treated,HCV-monoinfected [Group 3])	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	67	59	27	
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Wk 1(Group 1: N = 65;Group 2 = 58; Group 3: N =27)	-3.97 (± 0.675)	-4.34 (± 0.626)	-4.12 (± 0.582)	
Wk 2(Group 1: N = 67;Group 2 = 58; Group 3: N =27)	-4.5 (± 0.687)	-4.76 (± 0.522)	-4.83 (± 0.63)	
Wk 4	-4.74 (± 0.723)	-4.89 (± 0.534)	-5.08 (± 0.642)	
Wk 8	-4.74 (± 0.723)	-4.91 (± 0.536)	-5.11 (± 0.671)	
Wk 12	999 (± 999)	999 (± 999)	-5.11 (± 0.671)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Virologic Failure

End point title	Percentage of Participants With Virologic Failure

End point description:

1) Full Analysis Set
2) Virologic failure was defined as
• On-treatment virologic failure

• confirmed HCV RNA ≥ LLOQ after having previously had HCV RNA < LLOQ, while on treatment (ie, breakthrough),
• confirmed > 1 log10 IU/mL increase in HCV RNA from nadir while on treatment (ie, rebound), HCV RNA
persistently ≥ LLOQ through 8 weeks of treatment (ie, nonresponse)
• Relapse
• HCV RNA ≥ LLOQ during the posttreatment period having achieved HCV RNA < LLOQ at end of treatment,
confirmed with 2 consecutive values or last available posttreatment measurement

End point type	Secondary

End point timeframe:

Up to Posttreatment Week 24

End point values	LDV/SOF 8 Weeks (TN, HCV-monoinfected [Group 1])	LDV/SOF 8 Weeks (TN, HCV/HIV-coinfected [Group 2])	LDV/SOF+RBV 12 Wks (TE,SOF-treated,HCV-monoinfected [Group 3])	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	67	59	27	
Units: percentage of participants				
number (not applicable)	0	3.4	3.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of HIV/HCV-Coinfected Participants That Maintain HIV-1 RNA < 50 Copies/mL While on HCV Treatment and at Posttreatment Week 4

End point title	Percentage of HIV/HCV-Coinfected Participants That Maintain HIV-1 RNA < 50 Copies/mL While on HCV Treatment and at Posttreatment Week 4[3]

End point description:

Participants in the Safety Analysis Set (who had HIV RNA < 50 Copies/mL at baseline) with available data were analyzed.

End point type	Secondary

End point timeframe:

Up to Posttreatment Week 4

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This secondary endpoint was not analyzed for Group 1 and 3.

End point values	LDV/SOF 8 Weeks (TN, HCV/HIV-coinfected [Group 2])			
Subject group type	Reporting group			
Number of subjects analysed	45			
Units: percentage of participants				

number (not applicable)				
Week 4	100			
Week 8 (N= 43)	100			
Posttreatment Week 4 (N= 36)	97.2			

Statistical analyses

No statistical analyses for this end point

Secondary: For HIV/HCV-Coinfected Participants, Change From Baseline in CD4 T-cell Count at the End of Treatment and Posttreatment Week 4

End point title	For HIV/HCV-Coinfected Participants, Change From Baseline in CD4 T-cell Count at the End of Treatment and Posttreatment Week 4

End point description:

Participant in the Safety analysis set (with or without prior ARV treatment) with available data were analyzed.

End point type	Secondary

End point timeframe:

Up to Posttreatment Week 4

End point values	LDV/SOF 8 Weeks (TN, HCV/HIV-coinfected, ARV-Naive)	LDV/SOF 8 Weeks (TN, HCV/HIV-coinfected, ARV-Experienced)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44	9		
Units: cells/µL				
arithmetic mean (standard deviation)				
Wk 4 (ARV-Naive: N=43; ARV-Exp: N=9)	47 (± 120.5)	159 (± 114.9)		
Wk 8 (ARV-Naive: N=44; ARV-Exp: N=9)	45 (± 122.7)	202 (± 178.1)		
FU-Wk 4 (ARV-Naive: N=35; ARV-Exp: N=5)	74 (± 117.8)	172 (± 114.1)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 12 weeks plus 30 days	
Adverse event reporting additional description:	
Safety Analysis Set included all participants who received at least 1 dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups	
Reporting group title	LDV/SOF 8 Weeks (TN, HCV-monoinfected)
Reporting group description:	
LDV/SOF (90/400 mg) FDC tablet once daily for 8 weeks in treatment-naive (TN) participants with genotype 1 HCV infection without cirrhosis	
Reporting group title	LDV/SOF 8 Weeks (TN, HCV/HIV-coinfected)
Reporting group description:	
LDV/SOF (90/400 mg) FDC tablet once daily for 8 weeks in treatment naive participants with genotype 1 HCV infection without cirrhosis and coinfected with HIV-1	
Reporting group title	LDV/SOF + RBV 12 Weeks (TE, SOF-treated, HCV-monoinfected)
Reporting group description:	
LDV/SOF (90/400 mg) FDC tablet once daily + weight-based ribavirin (RBV) (1000-1200 mg in a divided daily dose) for 12 weeks in treatment-experienced (TE) participants with genotype 1 or 3 HCV infection who failed to achieve SVR in a previous Gilead sofosbuvir study	

Serious adverse events	LDV/SOF 8 Weeks (TN, HCV-monoinfected)	LDV/SOF 8 Weeks (TN, HCV/HIV-coinfected)	LDV/SOF + RBV 12 Weeks (TE, SOF-treated, HCV-monoinfected)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 67 (0.00%)	0 / 59 (0.00%)	0 / 27 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	LDV/SOF 8 Weeks (TN, HCV-monoinfected)	LDV/SOF 8 Weeks (TN, HCV/HIV-coinfected)	LDV/SOF + RBV 12 Weeks (TE, SOF-treated, HCV-monoinfected)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 67 (7.46%)	2 / 59 (3.39%)	8 / 27 (29.63%)
Investigations			

Blood bilirubin increased			
subjects affected / exposed	0 / 67 (0.00%)	0 / 59 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 67 (5.97%)	0 / 59 (0.00%)	4 / 27 (14.81%)
occurrences (all)	4	0	4
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 67 (1.49%)	0 / 59 (0.00%)	2 / 27 (7.41%)
occurrences (all)	1	0	2
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 67 (1.49%)	1 / 59 (1.69%)	2 / 27 (7.41%)
occurrences (all)	1	1	2
Dyspepsia			
subjects affected / exposed	0 / 67 (0.00%)	0 / 59 (0.00%)	3 / 27 (11.11%)
occurrences (all)	0	0	3
Psychiatric disorders			
Irritability			
subjects affected / exposed	0 / 67 (0.00%)	1 / 59 (1.69%)	2 / 27 (7.41%)
occurrences (all)	0	1	3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 June 2015	• Added Amiodarone to the "Agents Disallowed" list based on risk of symptomatic bradycardia with coadministration of amiodarone with ledipasvir/sofosbuvir. Postmarketing cases of symptomatic bradycardia were reported in patients receiving amiodarone who were coadministered Harvoni® (ledipasvir/sofosbuvir), or Sovaldi® (sofosbuvir) in combination with another direct acting antiviral. • Added information from the GS-US-337-0115 (ION-4) study (LDV/SOF in HCV/HIV co-infected subjects) • Added abacavir/lamivudine and dolutegravir as acceptable HIV ARV medications • Added optional additional testing to differentiate HIV-1 and HIV-2 infection to the laboratory tests to be performed as needed • Clarified inclusion/exclusion criteria related to Group 3 subjects (ie, subjects who failed to achieve SVR12 in study GS-US-334-0119) to o Allow enrolment of subjects who do not meet all laboratory requirements upon approval by the Gilead Medical Monitor or Study Director o Explicitly excluded subjects who did not participate in or who achieved SVR12 study GS-US-334-0119

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported