



Clinical trial results:

**A Phase 2, Multicenter, Open-Label Study to Evaluate the Efficacy and Safety of Ledipasvir/Sofosbuvir in Subjects with Genotype 1, 4, 5 and 6 Chronic HCV Infection Who are on Dialysis for End Stage Renal Disease
Summary**

EudraCT number	2016-003489-25
Trial protocol	BE IT
Global end of trial date	14 February 2019

Results information

Result version number	v1 (current)
This version publication date	02 December 2019
First version publication date	02 December 2019

Trial information

Trial identification

Sponsor protocol code	GS-US-337-4063
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03036839
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	14 February 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 October 2018
Global end of trial reached?	Yes
Global end of trial date	14 February 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study was to evaluate the safety, efficacy and tolerability of treatment with ledipasvir/sofosbuvir (LDV/SOF) in adults with chronic hepatitis C virus (HCV) infection who were on dialysis for end stage renal disease (ESRD).

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	27 June 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Italy: 16
Country: Number of subjects enrolled	United States: 8
Country: Number of subjects enrolled	Taiwan: 60
Worldwide total number of subjects	95
EEA total number of subjects	27

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)	56
From 65 to 84 years	39
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Taiwan, Italy, Germany, the United States, and Belgium. The first participant was screened on 27 June 2017. The last study visit occurred on 14 February 2019.

Pre-assignment

Screening details:

124 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 for 8 Weeks

Arm description:

Treatment-naïve genotype 1 participants without cirrhosis received LDV/SOF (90/400 mg) fixed-dose combination (FDC) tablet once daily orally with or without food for 8 weeks.

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

Dosage and administration details:

90/400 mg FDC administered once daily for 8 weeks.

Arm title	LDV/SOF for 12 Weeks
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Arm description:

Treatment-experienced genotype 1 participants and treatment-naïve or treatment-experienced genotype 2 (Taiwan only), 4, 5, and 6 participants without cirrhosis received LDV/SOF (90/400 mg) FDC tablet once daily orally with or without food for 12 weeks.

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

Dosage and administration details:

90/400 mg FDC administered once daily for 12 weeks.

Arm title	LDV/SOF for 24 Weeks
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Arm description:

Participants with compensated cirrhosis received LDV/SOF (90/400 mg) FDC tablet once daily orally with or without food for 24 weeks.

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

Dosage and administration details:

90/400 mg FDC administered once daily for 24 weeks.

Number of subjects in period 1	LDV/SOF for 8 Weeks	LDV/SOF for 12 Weeks	LDV/SOF for 24 Weeks
Started	45	31	19
Completed	42	31	14
Not completed	3	0	5
Withdrew Consent	-	-	1
Death	3	-	3
Adverse event	-	-	1

Baseline characteristics

Reporting groups

Reporting group title	LDV/SOF for 8 Weeks
Reporting group description: Treatment-naive genotype 1 participants without cirrhosis received LDV/SOF (90/400 mg) fixed-dose combination (FDC) tablet once daily orally with or without food for 8 weeks.	
Reporting group title	LDV/SOF for 12 Weeks
Reporting group description: Treatment-experienced genotype 1 participants and treatment-naive or treatment-experienced genotype 2 (Taiwan only), 4, 5, and 6 participants without cirrhosis received LDV/SOF (90/400 mg) FDC tablet once daily orally with or without food for 12 weeks.	
Reporting group title	LDV/SOF for 24 Weeks
Reporting group description: Participants with compensated cirrhosis received LDV/SOF (90/400 mg) FDC tablet once daily orally with or without food for 24 weeks.	

Reporting group values	LDV/SOF for 8 Weeks	LDV/SOF for 12 Weeks	LDV/SOF for 24 Weeks
Number of subjects	45	31	19
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	60	59	65
standard deviation	± 12.0	± 10.1	± 7.1
Gender categorical Units: Subjects			
Female	16	19	4
Male	29	12	15
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	2
Not Hispanic or Latino	45	31	17
Unknown or Not Reported	0	0	0
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	21	29	11
Native Hawaiian or Other Pacific Islander	1	0	0
Black or African American	3	0	2
White	20	2	6
More than one race	0	0	0
Unknown or Not Reported	0	0	0
IL28b Status			
The CC, CT, and TT alleles are different forms of the IL28b gene			
Units: Subjects			
CC	24	24	9

CT	12	5	9
TT	9	2	1
HCV RNA Category Units: Subjects			
< 800,000 IU/mL	24	14	10
≥ 800,000 IU/mL	21	17	9
Cirrhosis Status Units: Subjects			
Yes	0	0	19
No	45	31	0
HCV Genotype Units: Subjects			
Genotype 1	45	8	15
Genotype 2	0	19	2
Genotype 4	0	0	2
Genotype 5	0	1	0
Genotype 6	0	2	0
Indeterminate	0	1	0
HCV RNA Units: log10 IU/mL			
arithmetic mean	5.8	5.9	5.9
standard deviation	± 0.80	± 0.95	± 0.63

Reporting group values	Total		
Number of subjects	95		
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	39		
Male	56		
Ethnicity Units: Subjects			
Hispanic or Latino	2		
Not Hispanic or Latino	93		
Unknown or Not Reported	0		
Race Units: Subjects			
American Indian or Alaska Native	0		
Asian	61		
Native Hawaiian or Other Pacific Islander	1		
Black or African American	5		
White	28		
More than one race	0		
Unknown or Not Reported	0		

IL28b Status			
The CC, CT, and TT alleles are different forms of the IL28b gene			
Units: Subjects			
CC	57		
CT	26		
TT	12		
HCV RNA Category			
Units: Subjects			
< 800,000 IU/mL	48		
≥ 800,000 IU/mL	47		
Cirrhosis Status			
Units: Subjects			
Yes	19		
No	76		
HCV Genotype			
Units: Subjects			
Genotype 1	68		
Genotype 2	21		
Genotype 4	2		
Genotype 5	1		
Genotype 6	2		
Indeterminate	1		
HCV RNA			
Units: log ₁₀ IU/mL			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	LDV/SOF for 8 Weeks
Reporting group description: Treatment-naive genotype 1 participants without cirrhosis received LDV/SOF (90/400 mg) fixed-dose combination (FDC) tablet once daily orally with or without food for 8 weeks.	
Reporting group title	LDV/SOF for 12 Weeks
Reporting group description: Treatment-experienced genotype 1 participants and treatment-naive or treatment-experienced genotype 2 (Taiwan only), 4, 5, and 6 participants without cirrhosis received LDV/SOF (90/400 mg) FDC tablet once daily orally with or without food for 12 weeks.	
Reporting group title	LDV/SOF for 24 Weeks
Reporting group description: Participants with compensated cirrhosis received LDV/SOF (90/400 mg) FDC tablet once daily orally with or without food for 24 weeks.	

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

End point title	Percentage of Participants With Sustained Virologic Response (SVR) 12 Weeks After Discontinuation of Therapy (SVR12) ^[1]
End point description: SVR12 was defined as hepatitis C virus ribonucleic acid (HCV RNA) < the lower limit of quantitation (LLOQ; ie, 15 IU/mL) at 12 weeks after stopping study treatment. The exact 95% confidence interval (CI) for the percentage within treatment group was based on the Clopper-Pearson method. The Full Analysis Set (FAS) included participants who were enrolled into the study and received at least 1 dose of study drug. Participants were grouped within the Full Analysis Set by genotype and treatment group to which they were enrolled.	
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 for 8 Weeks	LDV/SOF for 12 Weeks	LDV/SOF for 24 Weeks	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	45	31	19	
Units: percentage of participants				
number (confidence interval 95%)	93.3 (81.7 to 98.6)	100.0 (88.8 to 100.0)	84.2 (60.4 to 96.6)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Permanently Discontinued Study Drug Due

to an Adverse Event

End point title	Percentage of Participants Who Permanently Discontinued Study Drug Due to an Adverse Event ^[2]
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End point description:

The Safety Analysis Set included all participants who received at least 1 dose of study drug. Participants were grouped within the Safety Analysis Set according to the treatment they actually received.

End point type	Primary
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End point timeframe:

First dose date up to Week 24

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 for 8 Weeks	LDV/SOF for 12 Weeks	LDV/SOF for 24 Weeks	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	45	31	19	
Units: percentage of participants				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With SVR at 4 Weeks After Discontinuation of Therapy (SVR4)

End point title	Percentage of Participants With SVR at 4 Weeks After Discontinuation of Therapy (SVR4)
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End point description:

SVR4 was defined as HCV RNA < LLOQ (ie, 15 IU/mL) at 4 weeks after stopping study treatment. The exact 95% CI for the percentage within treatment group was based on the Clopper-Pearson method. Participants in the Full Analysis Set were analyzed.

End point type	Secondary
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End point timeframe:

Posttreatment Week 4

End point values	LDV/SOF for 8 Weeks	LDV/SOF for 12 Weeks	LDV/SOF for 24 Weeks	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	45	31	19	
Units: percentage of participants				
number (confidence interval 95%)	97.8 (88.2 to 99.9)	100.0 (88.8 to 100.0)	84.2 (60.4 to 96.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With SVR at 24 Weeks After Discontinuation of Therapy (SVR24)

End point title | Percentage of Participants With SVR at 24 Weeks After Discontinuation of Therapy (SVR24)

End point description:

SVR24 was defined as HCV RNA < LLOQ (ie, 15 IU/mL) at 24 weeks after stopping study treatment. The exact 95% CI for the percentage within treatment group was based on the Clopper-Pearson method. Participants in the Full Analysis Set were analyzed.

End point type | Secondary

End point timeframe:

Posttreatment Week 24

End point values	LDV/SOF for 8 Weeks	LDV/SOF for 12 Weeks	LDV/SOF for 24 Weeks	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	45	31	19	
Units: percentage of participants				
number (confidence interval 95%)	93.3 (81.7 to 98.6)	100.0 (88.8 to 100.0)	84.2 (60.4 to 96.6)	

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:

The total number of participants with HCV RNA < LLOQ was the sum of the number of participants with HCV RNA "< LLOQ detected" plus the number of subjects with HCV RNA "< LLOQ target not detected (TND)". LLOQ was 15 IU/mL. The exact 95% CI for the percentage within treatment group was based on the Clopper-Pearson method. Participants in the Full Analysis Set with available data were analyzed. Here "n" signified number of participants analyzed for the specific timepoint and "99999" signified data were not applicable to be reported, since no participant was analyzed in the specific timepoint for the respective arm.

End point type | Secondary

End point timeframe:

Weeks 2, 4, 6, 8, 12, 16, 20, 24

End point values	LDV/SOF for 8 Weeks	LDV/SOF for 12 Weeks	LDV/SOF for 24 Weeks	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	45	31	19	
Units: percentage of participants				
number (confidence interval 95%)				

Week 2 (n= 45, 31, 19)	84.4 (70.5 to 93.5)	90.3 (74.2 to 98.0)	84.2 (60.4 to 96.6)
Week 4 (n= 44, 31, 19)	100.0 (92.0 to 100.0)	100.0 (88.8 to 100.0)	100.0 (82.4 to 100.0)
Week 6 (n= 44, 31, 19)	100.0 (92.0 to 100.0)	100.0 (88.8 to 100.0)	94.7 (74.0 to 99.9)
Week 8 (n= 44, 31, 18)	100.0 (92.0 to 100.0)	100.0 (88.8 to 100.0)	100.0 (81.5 to 100.0)
Week 12 (n= 0, 31, 17)	99999 (99999 to 99999)	100.0 (88.8 to 100.0)	100.0 (80.5 to 100.0)
Week 16 (n= 0, 0, 17)	99999 (99999 to 99999)	99999 (99999 to 99999)	100.0 (80.5 to 100.0)
Week 20 (n= 0, 0, 17)	99999 (99999 to 99999)	99999 (99999 to 99999)	100.0 (80.5 to 100.0)
Week 24 (n= 0, 0, 16)	99999 (99999 to 99999)	99999 (99999 to 99999)	100.0 (79.4 to 100.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in HCV RNA

End point title	Change From Baseline in HCV RNA
End point description:	
Participants in the Full Analysis Set with available data were analyzed. Here "n" signified number of participants analyzed for the specific timepoint and "99999" signified data were not applicable to be reported, since no participant was analyzed in the specific timepoint for the respective arm.	
End point type	Secondary
End point timeframe:	
Weeks 2, 4, 6, 8, 12, 16, 20, 24	

End point values	LDV/SOF for 8 Weeks	LDV/SOF for 12 Weeks	LDV/SOF for 24 Weeks
Subject group type	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	31	19
Units: log ₁₀ IU/mL			
arithmetic mean (standard deviation)			
Change at Week 2 (n= 42, 31, 19)	-4.63 (± 0.799)	-4.71 (± 0.894)	-4.67 (± 0.631)
Change at Week 4 (n= 44, 31, 19)	-4.61 (± 0.805)	-4.79 (± 0.950)	-4.71 (± 0.631)
Change at Week 6 (n= 44, 31, 18)	-4.61 (± 0.805)	-4.79 (± 0.950)	-4.81 (± 0.474)
Change at Week 8 (n= 44, 31, 18)	-4.61 (± 0.805)	-4.79 (± 0.950)	-4.81 (± 0.474)
Change at Week 12 (n= 0, 31, 17)	99999 (± 99999)	-4.79 (± 0.950)	-4.79 (± 0.480)
Change at Week 16 (n= 0, 0, 17)	99999 (± 99999)	99999 (± 99999)	-4.79 (± 0.480)
Change at Week 20 (n= 0, 0, 17)	99999 (± 99999)	99999 (± 99999)	-4.79 (± 0.480)

Change at Week 24 (n= 0, 0, 16)	99999 (± 99999)	99999 (± 99999)	-4.75 (± 0.466)	
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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
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End point description:

Virologic failure was defined as:

- On-treatment virologic failure:
- Breakthrough (confirmed HCV RNA \geq LLOQ after having previously had HCV RNA $<$ LLOQ while on treatment), or
- Rebound (confirmed > 1 log₁₀ IU/mL increase in HCV RNA from nadir while on treatment), or
- Non-response (HCV RNA persistently \geq LLOQ through 8 weeks of treatment)
- Virologic relapse:
- Confirmed HCV RNA \geq LLOQ during the posttreatment period having achieved HCV RNA $<$ LLOQ at last ontreatment visit.

Participants in the Full Analysis Set were analyzed.

End point type	Secondary
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End point timeframe:

Baseline up to Posttreatment Week 24

End point values	LDV/SOF for 8 Weeks	LDV/SOF for 12 Weeks	LDV/SOF for 24 Weeks	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	45	31	19	
Units: percentage of participants				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Developed Resistance to LDV and SOF

End point title	Percentage of Participants Who Developed Resistance to LDV and SOF
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End point description:

The Resistance Analysis Population was defined as all participants in the Safety Analysis Set with a virologic outcome and at least 1 gene sequenced. As no participant had a relapse in this study, this outcome could not be analyzed.

End point type	Secondary
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End point timeframe:

Baseline up to Posttreatment Week 24

End point values	LDV/SOF for 8 Weeks	LDV/SOF for 12 Weeks	LDV/SOF for 24 Weeks	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[3]	0 ^[4]	0 ^[5]	
Units: percentage of participants				
number (not applicable)				

Notes:

[3] - Since no participants had virologic outcome, hence, no participants were analyzed for the endpoint.

[4] - Since no participants had virologic outcome, hence, no participants were analyzed for the endpoint.

[5] - Since no participants had virologic outcome, hence, no participants were analyzed for the endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK) Parameter: AUCtau of LDV

End point title	Pharmacokinetics (PK) Parameter: AUCtau of LDV
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End point description:

AUCtau is defined as the population PK derived area under the concentration versus time curve of the drug over the dosing interval. The PK Analysis Set included all participants who took at least 1 dose of the study drug and had at least 1 nonmissing postdose concentration value for the corresponding analyte in plasma.

End point type	Secondary
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End point timeframe:

Sparse PK Samples at Weeks 6, 8, and 12 (all participants). Intensive PK samples at predose, 0.25, 0.5, 1, 2, 4, 6, 8, 10, and 12 hours postdose once at Weeks 6, 8, or 12 (participants who enrolled in the optional PK substudy (N=2))

End point values	LDV/SOF for 8 Weeks	LDV/SOF for 12 Weeks	LDV/SOF for 24 Weeks	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	44	31	19	
Units: h*ng/mL				
arithmetic mean (standard deviation)	11923.9 (± 6319.41)	13632.7 (± 4648.74)	13542.5 (± 6322.88)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: AUCtau of SOF

End point title	PK Parameter: AUCtau of SOF
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End point description:

AUCtau is defined as the population PK derived area under the concentration versus time curve of the drug over the dosing interval. Participants in the PK Analysis Set with available data were analyzed.

End point type	Secondary
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End point timeframe:

Sparse PK Samples at Weeks 6, 8, and 12 (all participants). Intensive PK samples at predose, 0.25, 0.5, 1, 2, 4, 6, 8, 10, and 12 hours postdose once at Weeks 6, 8, or 12 (participants who enrolled in the optional PK substudy (N=2))

End point values	LDV/SOF for 8 Weeks	LDV/SOF for 12 Weeks	LDV/SOF for 24 Weeks	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	23	12	
Units: h*ng/mL				
arithmetic mean (standard deviation)	2435.4 (± 452.83)	2296.6 (± 583.30)	2838.2 (± 438.93)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: AUCtau of GS-331007 (Metabolite of SOF)

End point title	PK Parameter: AUCtau of GS-331007 (Metabolite of SOF)
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End point description:

AUCtau is defined as the population PK derived area under the concentration versus time curve of the drug over the dosing interval. Participants in the PK Analysis Set were analyzed.

End point type	Secondary
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End point timeframe:

Sparse PK Samples at Weeks 6, 8, and 12 (all participants). Intensive PK samples at predose, 0.25, 0.5, 1, 2, 4, 6, 8, 10, and 12 hours postdose once at Weeks 6, 8, or 12 (participants who enrolled in the optional PK substudy (N=2))

End point values	LDV/SOF for 8 Weeks	LDV/SOF for 12 Weeks	LDV/SOF for 24 Weeks	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	44	31	19	
Units: h*ng/mL				
arithmetic mean (standard deviation)	234980.1 (± 67648.52)	269050.3 (± 93600.65)	280829.5 (± 93618.16)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Cmax of LDV

End point title	PK Parameter: Cmax of LDV
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End point description:

C_{max} is defined as the population PK derived maximum concentration of the drug. Participants in the PK Analysis Set were analyzed.

End point type Secondary

End point timeframe:

Sparse PK Samples at Weeks 6, 8, and 12 (all participants). Intensive PK samples at predose, 0.25, 0.5, 1, 2, 4, 6, 8, 10, and 12 hours postdose once at Weeks 6, 8, or 12 (participants who enrolled in the optional PK substudy (N=2))

End point values	LDV/SOF for 8 Weeks	LDV/SOF for 12 Weeks	LDV/SOF for 24 Weeks	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	44	31	19	
Units: ng/mL				
arithmetic mean (standard deviation)	544.2 (± 271.72)	618.4 (± 204.87)	607.0 (± 267.38)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: C_{max} of SOF

End point title PK Parameter: C_{max} of SOF

End point description:

C_{max} is defined as the population PK derived maximum concentration of the drug. Participants in the PK Analysis Set with available data were analyzed.

End point type Secondary

End point timeframe:

Sparse PK Samples at Weeks 6, 8, and 12 (all participants). Intensive PK samples at predose, 0.25, 0.5, 1, 2, 4, 6, 8, 10, and 12 hours postdose once at Weeks 6, 8, or 12 (participants who enrolled in the optional PK substudy (N=2))

End point values	LDV/SOF for 8 Weeks	LDV/SOF for 12 Weeks	LDV/SOF for 24 Weeks	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	23	12	
Units: ng/mL				
arithmetic mean (standard deviation)	1059.8 (± 251.74)	1005.8 (± 204.54)	1052.5 (± 295.06)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Cmax of GS-331007 (Metabolite of SOF)

End point title	PK Parameter: Cmax of GS-331007 (Metabolite of SOF)
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End point description:

Cmax is defined as the population PK derived maximum concentration of the drug. Participants in the PK Analysis Set were analyzed.

End point type	Secondary
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End point timeframe:

Sparse PK Samples at Weeks 6, 8, and 12 (all participants). Intensive PK samples at predose, 0.25, 0.5, 1, 2, 4, 6, 8, 10, and 12 hours postdose once at Weeks 6, 8, or 12 (participants who enrolled in the optional PK substudy (N=2))

End point values	LDV/SOF for 8 Weeks	LDV/SOF for 12 Weeks	LDV/SOF for 24 Weeks	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	44	31	19	
Units: ng/mL				
arithmetic mean (standard deviation)	9956.3 (± 2846.07)	11392.7 (± 3938.33)	11882.4 (± 3951.04)	

Statistical analyses

No statistical analyses for this end point

Secondary: HCV-RNA

End point title	HCV-RNA
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End point description:

Participants in the Full Analysis Set with available data were analyzed. Here "n" signified number of participants analyzed for the specific timepoint and "99999" signified data were not applicable to be reported, since no participant was analyzed in the specific timepoint for the respective arm.

End point type	Secondary
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End point timeframe:

Weeks 2, 4, 6, 8, 12, 16, 20, 24

End point values	LDV/SOF for 8 Weeks	LDV/SOF for 12 Weeks	LDV/SOF for 24 Weeks	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	44	31	19	
Units: log ₁₀ IU/mL				
arithmetic mean (standard deviation)				
Week 2 (n= 42, 31, 19)	1.17 (± 0.107)	1.22 (± 0.261)	1.18 (± 0.098)	
Week 4 (n= 44, 31, 19)	1.15 (± 0.000)	1.15 (± 0.000)	1.15 (± 0.000)	
Week 6 (n= 44, 31, 18)	1.15 (± 0.000)	1.15 (± 0.000)	1.15 (± 0.000)	
Week 8 (n= 44, 31, 18)	1.15 (± 0.000)	1.15 (± 0.000)	1.15 (± 0.000)	
Week 12 (n= 0, 31, 17)	99999 (± 99999)	1.15 (± 0.000)	1.15 (± 0.000)	

Week 16 (n= 0, 0, 17)	99999 (± 99999)	99999 (± 99999)	1.15 (± 0.000)	
Week 20 (n= 0, 0, 17)	99999 (± 99999)	99999 (± 99999)	1.15 (± 0.000)	
Week 24(n= 0, 0, 16)	99999 (± 99999)	99999 (± 99999)	1.15 (± 0.000)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

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

Adverse event reporting additional description:

The Safety Analysis Set included all participants who received at least 1 dose of study drug. Participants were grouped within the Safety Analysis Set according to the treatment they actually received.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.1
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Reporting groups

Reporting group title	LDV/SOF for 8 Weeks
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Reporting group description:

Treatment-naive genotype 1 participants without cirrhosis received ledipasvir/sofosbuvir (LDV/SOF) (90/400 mg) fixed-dose combination (FDC) tablet once daily orally with or without food for 8 weeks.

Reporting group title	LDV/SOF for 12 Weeks
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Reporting group description:

Treatment-experienced genotype 1 participants and treatment-naive or treatment-experienced genotype 2 (Taiwan only), 4, 5, and 6 participants without cirrhosis received LDV/SOF (90/400 mg) FDC tablet once daily orally with or without food for 12 weeks.

Reporting group title	LDV/SOF for 24 Weeks
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Reporting group description:

Participants with compensated cirrhosis received LDV/SOF (90/400 mg) FDC tablet once daily orally with or without food for 24 weeks.

Serious adverse events	LDV/SOF for 8 Weeks	LDV/SOF for 12 Weeks	LDV/SOF for 24 Weeks
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 45 (8.89%)	2 / 31 (6.45%)	6 / 19 (31.58%)
number of deaths (all causes)	3	0	3
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatocellular carcinoma			
subjects affected / exposed	0 / 45 (0.00%)	1 / 31 (3.23%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Accidental overdose			

subjects affected / exposed	1 / 45 (2.22%)	0 / 31 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriovenous fistula site complication			
subjects affected / exposed	0 / 45 (0.00%)	1 / 31 (3.23%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriovenous fistula thrombosis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 31 (3.23%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 45 (0.00%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	1 / 45 (2.22%)	0 / 31 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 45 (0.00%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac valve disease			
subjects affected / exposed	0 / 45 (0.00%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 45 (2.22%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Gastrointestinal disorders			
Duodenal ulcer haemorrhage			
subjects affected / exposed	1 / 45 (2.22%)	0 / 31 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic erosive gastritis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melaena			
subjects affected / exposed	0 / 45 (0.00%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatitis acute			
subjects affected / exposed	0 / 45 (0.00%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 45 (0.00%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Psychiatric disorders			
Mental status changes			

subjects affected / exposed	1 / 45 (2.22%)	0 / 31 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Infection			
subjects affected / exposed	1 / 45 (2.22%)	0 / 31 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 31 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	LDV/SOF for 8 Weeks	LDV/SOF for 12 Weeks	LDV/SOF for 24 Weeks
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 45 (51.11%)	28 / 31 (90.32%)	15 / 19 (78.95%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 45 (0.00%)	1 / 31 (3.23%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Hypotension			
subjects affected / exposed	0 / 45 (0.00%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	3 / 45 (6.67%)	2 / 31 (6.45%)	2 / 19 (10.53%)
occurrences (all)	3	2	2
Asthenia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 31 (0.00%)	4 / 19 (21.05%)
occurrences (all)	1	0	4
Pyrexia			
subjects affected / exposed	1 / 45 (2.22%)	1 / 31 (3.23%)	1 / 19 (5.26%)
occurrences (all)	1	1	1
Chest discomfort			
subjects affected / exposed	0 / 45 (0.00%)	1 / 31 (3.23%)	1 / 19 (5.26%)
occurrences (all)	0	1	3
Chest pain			
subjects affected / exposed	0 / 45 (0.00%)	1 / 31 (3.23%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Influenza like illness			
subjects affected / exposed	1 / 45 (2.22%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Oedema peripheral			
subjects affected / exposed	0 / 45 (0.00%)	1 / 31 (3.23%)	1 / 19 (5.26%)
occurrences (all)	0	2	3
Tenderness			
subjects affected / exposed	0 / 45 (0.00%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 45 (6.67%)	3 / 31 (9.68%)	0 / 19 (0.00%)
occurrences (all)	3	3	0
Dyspnoea			
subjects affected / exposed	0 / 45 (0.00%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 45 (2.22%)	4 / 31 (12.90%)	1 / 19 (5.26%)
occurrences (all)	1	4	1
Injury, poisoning and procedural complications			

Contusion			
subjects affected / exposed	1 / 45 (2.22%)	2 / 31 (6.45%)	3 / 19 (15.79%)
occurrences (all)	2	2	3
Fall			
subjects affected / exposed	0 / 45 (0.00%)	3 / 31 (9.68%)	1 / 19 (5.26%)
occurrences (all)	0	3	1
Shunt occlusion			
subjects affected / exposed	3 / 45 (6.67%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences (all)	3	0	4
Limb injury			
subjects affected / exposed	0 / 45 (0.00%)	1 / 31 (3.23%)	2 / 19 (10.53%)
occurrences (all)	0	2	2
Muscle strain			
subjects affected / exposed	1 / 45 (2.22%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Concussion			
subjects affected / exposed	0 / 45 (0.00%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Ligament sprain			
subjects affected / exposed	0 / 45 (0.00%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Shunt stenosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 45 (0.00%)	1 / 31 (3.23%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Atrial fibrillation			
subjects affected / exposed	0 / 45 (0.00%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Cardiac valve disease			
subjects affected / exposed	0 / 45 (0.00%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Myocardial ischaemia			

subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 31 (0.00%) 0	1 / 19 (5.26%) 1
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 45 (6.67%)	3 / 31 (9.68%)	2 / 19 (10.53%)
occurrences (all)	4	3	2
Dizziness			
subjects affected / exposed	2 / 45 (4.44%)	4 / 31 (12.90%)	1 / 19 (5.26%)
occurrences (all)	2	5	1
Hypoaesthesia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 45 (0.00%)	1 / 31 (3.23%)	1 / 19 (5.26%)
occurrences (all)	0	1	2
Eye disorders			
Cataract			
subjects affected / exposed	0 / 45 (0.00%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Conjunctival hyperaemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Glaucoma			
subjects affected / exposed	0 / 45 (0.00%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 45 (2.22%)	4 / 31 (12.90%)	1 / 19 (5.26%)
occurrences (all)	1	4	2
Nausea			
subjects affected / exposed	4 / 45 (8.89%)	1 / 31 (3.23%)	1 / 19 (5.26%)
occurrences (all)	5	1	1
Vomiting			
subjects affected / exposed	4 / 45 (8.89%)	1 / 31 (3.23%)	1 / 19 (5.26%)
occurrences (all)	4	1	1
Diarrhoea			

subjects affected / exposed	2 / 45 (4.44%)	2 / 31 (6.45%)	0 / 19 (0.00%)
occurrences (all)	2	2	0
Abdominal distension			
subjects affected / exposed	0 / 45 (0.00%)	2 / 31 (6.45%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Gastroesophageal reflux disease			
subjects affected / exposed	0 / 45 (0.00%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Hyperchlorhydria			
subjects affected / exposed	0 / 45 (0.00%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Large intestine polyp			
subjects affected / exposed	0 / 45 (0.00%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 45 (2.22%)	3 / 31 (9.68%)	3 / 19 (15.79%)
occurrences (all)	1	3	4
Rash			
subjects affected / exposed	0 / 45 (0.00%)	1 / 31 (3.23%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Ecchymosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Rash papular			
subjects affected / exposed	0 / 45 (0.00%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Skin exfoliation			
subjects affected / exposed	0 / 45 (0.00%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	1 / 45 (2.22%)	7 / 31 (22.58%)	4 / 19 (21.05%)
occurrences (all)	1	12	5
Arthralgia			

subjects affected / exposed occurrences (all)	2 / 45 (4.44%) 2	1 / 31 (3.23%) 1	1 / 19 (5.26%) 1
Arthritis			
subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	2 / 31 (6.45%) 2	0 / 19 (0.00%) 0
Musculoskeletal pain			
subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	1 / 31 (3.23%) 1	1 / 19 (5.26%) 1
Musculoskeletal chest pain			
subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 31 (0.00%) 0	1 / 19 (5.26%) 1
Myalgia			
subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 31 (0.00%) 0	1 / 19 (5.26%) 1
Pain in extremity			
subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 31 (0.00%) 0	1 / 19 (5.26%) 1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 3	7 / 31 (22.58%) 9	1 / 19 (5.26%) 1
Upper respiratory tract infection			
subjects affected / exposed occurrences (all)	2 / 45 (4.44%) 2	3 / 31 (9.68%) 4	0 / 19 (0.00%) 0
Cellulitis			
subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	2 / 31 (6.45%) 2	0 / 19 (0.00%) 0
Shunt infection			
subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1	0 / 31 (0.00%) 0	1 / 19 (5.26%) 1
Clostridial infection			
subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 31 (0.00%) 0	1 / 19 (5.26%) 1
Peritonitis bacterial			
subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 31 (0.00%) 0	1 / 19 (5.26%) 1

Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 45 (0.00%)	1 / 31 (3.23%)	1 / 19 (5.26%)
occurrences (all)	0	2	1
Hyperkalaemia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 31 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 November 2016	<ul style="list-style-type: none">- Update to the hemodialysis PK substudy design (removal of dialysate collection)- Clarification of the study drug dispensing schedules- Clarification of collection of information relating to PK samples, including time of prior dosing and time of prior dialysis.- Addition of an inclusion criterion that the most recent HCV treatment must have been completed at least 8 weeks prior to screening
30 January 2017	<ul style="list-style-type: none">- Addition of hepatitis B core antibody (HBcAb) and hepatitis B surface antibody (HBsAb) testing at screening and hepatitis B virus (HBV) deoxyribonucleic acid (DNA) testing for HBcAb+ participants at baseline/Day 1, every 4 weeks on-treatment and at posttreatment Weeks 4, 12 and 24- Change and clarification for timing of Data Monitoring Committee (DMC) meetings: initial review of data after the first 12 subjects completed 8 weeks of treatment, or early termination, and every 3 months thereafter. These subsequent safety reviews were to alternate between:<ul style="list-style-type: none">-A review by the DMC chair of all serious adverse events (SAEs) and deaths-A review of safety data by the DMC meeting as specified in the DMC charter- Addition of North America as a participating region, and an increase in the number of centers from approximately 35 to approximately 40- Addition of ClinicalTrials.gov identifier and IND number to the protocol cover page and synopsis- Addition of the term 'on dialysis for ESRD' to the exploratory objectives to keep consistency with the protocol title
02 March 2017	<ul style="list-style-type: none">-Communication to investigators the potential for hematologic toxicity associated with higher exposure of GS-331007, a metabolite of SOF.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported