Clinical trial results:
A Phase 2, Multicenter, Open-Label Study to Evaluate the Efficacy and Safety of Sofosbuvir/Velpatasvir for 12 Weeks in Subjects With Chronic HCV Infection Who Are on Dialysis for End Stage Renal Disease

Summary

EudraCT number	2016-003625-42
Trial protocol	GB ES
Global end of trial date	07 November 2018

Results information

Result version number	v1 (current)
This version publication date	27 November 2019
First version publication date	27 November 2019

Trial information

Trial identification

Sponsor protocol code	GS-US-342-4062

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03036852
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	07 November 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 August 2018
Global end of trial reached?	Yes
Global end of trial date	07 November 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study were to evaluate safety, efficacy, and tolerability of treatment with sofosbuvir/velpatasvir (SOF/VEL) fixed-dose combination (FDC) for 12 weeks in adults on dialysis for end stage renal disease (ESRD) with chronic hepatitis C virus (HCV) infection of any genotype.

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	22 March 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	United Kingdom: 16
Country: Number of subjects enrolled	Canada: 25
Country: Number of subjects enrolled	Israel: 6
Country: Number of subjects enrolled	New Zealand: 4
Country: Number of subjects enrolled	Australia: 2
Worldwide total number of subjects	59
EEA total number of subjects	22

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)	39
From 65 to 84 years	18
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Canada, the United Kingdom, Spain, Israel, New Zealand, and Australia. The first participant was screened on 22 March 2017. The last study visit occurred on 07 November 2018.

Pre-assignment

Screening details:

78 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

Arm title	SOF/VEL

Arm description:

SOF/VEL (400/100 mg) FDC tablet orally once daily for 12 weeks

Arm type	Experimental
Investigational medicinal product name	Sofosbuvir/Velpatasvir
Investigational medicinal product code	
Other name	SOF/VEL; Epclusa®; GS-7977/GS-5816
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

400/100 mg administered orally once daily

Number of subjects in period 1	SOF/VEL
Started	59
Completed	53
Not completed	6
Adverse event, non-fatal	1
Death	2
Lost to follow-up	1
Lack of efficacy	2

Baseline characteristics

Reporting groups	
Reporting group title	SOF/VEL
Reporting group description:	
SOF/VEL (400/100 mg) FDC tablet orally once daily for 12 weeks	

Reporting group values	SOF/VEL	Total	
Number of subjects	59	59	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	60		
standard deviation	± 12.1	-	
Gender categorical Units: Subjects			
Female	24	24	
Male	35	35	
Ethnicity Units: Subjects			
Hispanic or Latino	3	3	
Not Hispanic or Latino	56	56	
Race Units: Subjects			
American Indian or Alaska Native	2	2	
Asian	18	18	
Native Hawaiian or Other Pacific Islander	2	2	
Black or African American	6	6	
White	31	31	
IL28b Status Units: Subjects			
CC	23	23	
CT	30	30	
TT	6	6	
HCV RNA Category Units: Subjects			
< 800,000 IU/mL	26	26	
≥ 800,000 IU/mL	33	33	
HCV RNA Units: log10 IU/mL			
arithmetic mean	5.8		
standard deviation	± 1.02	-	

Subject analysis sets	
Subject analysis set title	SOF/VEL (GT-1)
Subject analysis set type	Safety analysis
Subject analysis set description:	
SOF/VEL (400/100 mg) FDC tablet orally once daily for 12 weeks in participants with genotype 1 (GT-1) HCV infection	
Subject analysis set title	SOF/VEL (GT-2)
Subject analysis set type	Safety analysis
Subject analysis set description:	
SOF/VEL (400/100 mg) FDC tablet orally once daily for 12 weeks in participants with genotype 2 (GT-2) HCV infection	
Subject analysis set title	SOF/VEL (GT-3)
Subject analysis set type	Safety analysis
Subject analysis set description:	
SOF/VEL (400/100 mg) FDC tablet orally once daily for 12 weeks in participants with genotype 3 (GT-3) HCV infection	
Subject analysis set title	SOF/VEL (GT-4)
Subject analysis set type	Safety analysis
Subject analysis set description:	
SOF/VEL (400/100 mg) FDC tablet orally once daily for 12 weeks in participants with genotype 4 (GT-4) HCV infection	
Subject analysis set title	SOF/VEL (GT-6)
Subject analysis set type	Safety analysis
Subject analysis set description:	
SOF/VEL (400/100 mg) FDC tablet orally once daily for 12 weeks in participants with genotype 6 (GT-6) HCV infection	
Subject analysis set title	SOF/VEL (Indeterminate)
Subject analysis set type	Safety analysis
Subject analysis set description:	
SOF/VEL (400/100 mg) FDC tablet orally once daily for 12 weeks in participants with indeterminate genotype HCV infection	

Reporting group values	SOF/VEL (GT-1)	SOF/VEL (GT-2)	SOF/VEL (GT-3)
Number of subjects	25	7	16
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	63	67	55
standard deviation	± 11.9	± 13.5	± 8.4
Gender categorical Units: Subjects			
Female	10	4	5
Male	15	3	11
Ethnicity Units: Subjects			
Hispanic or Latino	2	0	0
Not Hispanic or Latino	23	7	16
Race Units: Subjects			
American Indian or Alaska Native	1	0	1
Asian	6	1	7

Native Hawaiian or Other Pacific Islander	1	0	1
Black or African American	1	2	0
White	16	4	7
IL28b Status Units: Subjects			
CC	9	4	6
CT	14	1	8
TT	2	2	2
HCV RNA Category Units: Subjects			
< 800,000 IU/mL	12	5	4
≥ 800,000 IU/mL	13	2	12
HCV RNA Units: log10 IU/mL			
arithmetic mean	6.0	5.2	6.4
standard deviation	± 0.70	± 1.04	± 0.55

Reporting group values	SOF/VEL (GT-4)	SOF/VEL (GT-6)	SOF/VEL (Indeterminate)
Number of subjects	4	2	5
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	58	69	52
standard deviation	± 15.5	± 3.5	± 13.0
Gender categorical Units: Subjects			
Female	1	1	3
Male	3	1	2
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	1
Not Hispanic or Latino	4	2	4
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	2	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	0	1
White	1	0	3
IL28b Status Units: Subjects			
CC	0	1	3
CT	4	1	2
TT	0	0	0
HCV RNA Category Units: Subjects			
< 800,000 IU/mL	2	0	3

≥ 800,000 IU/mL	2	2	2

HCV RNA			
Units: log10 IU/mL			
arithmetic mean	5.6	6.4	4.4
standard deviation	± 1.55	± 0.27	± 1.69

End points

End points reporting groups

Reporting group title	SOF/VEL
Reporting group description: SOF/VEL (400/100 mg) FDC tablet orally once daily for 12 weeks	
Subject analysis set title	SOF/VEL (GT-1)
Subject analysis set type	Safety analysis
Subject analysis set description: SOF/VEL (400/100 mg) FDC tablet orally once daily for 12 weeks in participants with genotype 1 (GT-1) HCV infection	
Subject analysis set title	SOF/VEL (GT-2)
Subject analysis set type	Safety analysis
Subject analysis set description: SOF/VEL (400/100 mg) FDC tablet orally once daily for 12 weeks in participants with genotype 2 (GT-2) HCV infection	
Subject analysis set title	SOF/VEL (GT-3)
Subject analysis set type	Safety analysis
Subject analysis set description: SOF/VEL (400/100 mg) FDC tablet orally once daily for 12 weeks in participants with genotype 3 (GT-3) HCV infection	
Subject analysis set title	SOF/VEL (GT-4)
Subject analysis set type	Safety analysis
Subject analysis set description: SOF/VEL (400/100 mg) FDC tablet orally once daily for 12 weeks in participants with genotype 4 (GT-4) HCV infection	
Subject analysis set title	SOF/VEL (GT-6)
Subject analysis set type	Safety analysis
Subject analysis set description: SOF/VEL (400/100 mg) FDC tablet orally once daily for 12 weeks in participants with genotype 6 (GT-6) HCV infection	
Subject analysis set title	SOF/VEL (Indeterminate)
Subject analysis set type	Safety analysis
Subject analysis set description: SOF/VEL (400/100 mg) FDC tablet orally once daily for 12 weeks in participants with indeterminate genotype HCV infection	

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: SVR12 was defined as HCV RNA < the lower limit of quantitation (LLOQ; ie, 15 IU/mL) 12 weeks after stopping study treatment.The Full Analysis Set included participants who 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	SOF/VEL	SOF/VEL (GT-1)	SOF/VEL (GT-2)	SOF/VEL (GT-3)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	59	25	7	16
Units: Percentage of participants				
number (confidence interval 95%)	94.9 (85.9 to 98.9)	92.0 (74.0 to 99.0)	100.0 (59.0 to 100.0)	93.8 (69.8 to 99.8)

End point values	SOF/VEL (GT-4)	SOF/VEL (GT-6)	SOF/VEL (Indeterminate)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	2	5	
Units: Percentage of participants				
number (confidence interval 95%)	100.0 (39.8 to 100.0)	100.0 (15.8 to 100.0)	100.0 (47.8 to 100.0)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Permanently Discontinued the Study Drug Due to an Adverse Event

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

End point description:

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

End point type	Primary

End point timeframe:

First dose date up to Week 12

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	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	59			
Units: Percentage of participants				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Sustained Virologic Response 4 Weeks

After Discontinuation of Therapy (SVR4)

End point title	Percentage of Participants With Sustained Virologic Response 4 Weeks After Discontinuation of Therapy (SVR4)

End point description:

SVR4 was defined as HCV RNA < LLOQ 4 weeks after stopping study treatment. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Posttreatment Week 4

End point values	SOF/VEL	SOF/VEL (GT-1)	SOF/VEL (GT-2)	SOF/VEL (GT-3)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	59	25	7	16
Units: Percentage of participants				
number (confidence interval 95%)	96.6 (88.3 to 99.6)	96.0 (79.6 to 99.9)	100.0 (59.0 to 100.0)	93.8 (69.8 to 99.8)

End point values	SOF/VEL (GT-4)	SOF/VEL (GT-6)	SOF/VEL (Indeterminate)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	2	5	
Units: Percentage of participants				
number (confidence interval 95%)	100.0 (39.8 to 100.0)	100.0 (15.8 to 100.0)	100.0 (47.8 to 100.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Sustained Virologic Response 24 Weeks After Discontinuation of Therapy (SVR24)

End point title	Percentage of Participants With Sustained Virologic Response 24 Weeks After Discontinuation of Therapy (SVR24)

End point description:

SVR24 was defined as HCV RNA < LLOQ 24 weeks after stopping study treatment. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Posttreatment Week 24

End point values	SOF/VEL	SOF/VEL (GT-1)	SOF/VEL (GT-2)	SOF/VEL (GT-3)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	59	25	7	16
Units: Percentage of participants				
number (confidence interval 95%)	94.9 (85.9 to 98.9)	92.0 (74.0 to 99.0)	100.0 (59.0 to 100.0)	93.8 (69.8 to 99.8)

End point values	SOF/VEL (GT-4)	SOF/VEL (GT-6)	SOF/VEL (Indeterminate)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	2	5	
Units: Percentage of participants				
number (confidence interval 95%)	100.0 (39.8 to 100.0)	100.0 (15.8 to 100.0)	100.0 (47.8 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.	
End point type	Secondary
End point timeframe:	
Baseline; Weeks 2, 4, 6, 8, and 12	

End point values	SOF/VEL	SOF/VEL (GT-1)	SOF/VEL (GT-2)	SOF/VEL (GT-3)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	59	25	7	16
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Change at Week 2 (N = 59, 25, 6, 13, 4, 2, 5)	-4.54 (± 1.017)	-4.69 (± 0.797)	-3.78 (± 0.840)	-5.07 (± 0.493)
Change at Week 4 (N = 59, 25, 7, 16, 4, 2, 5)	-4.69 (± 1.020)	-4.81 (± 0.704)	-4.05 (± 1.041)	-5.20 (± 0.551)
Change at Week 6 (N = 59, 25, 7, 16, 4, 2, 5)	-4.69 (± 1.020)	-4.81 (± 0.704)	-4.05 (± 1.041)	-5.20 (± 0.551)
Change at Week 8 (N = 59, 25, 7, 16, 4, 2, 5)	-4.69 (± 1.020)	-4.81 (± 0.704)	-4.05 (± 1.041)	-5.20 (± 0.551)
Change at Week 12 (N = 59, 25, 7, 16, 4, 2, 5)	-4.69 (± 1.020)	-4.81 (± 0.704)	-4.05 (± 1.041)	-5.20 (± 0.551)

End point values	SOF/VEL (GT-4)	SOF/VEL (GT-6)	SOF/VEL (Indeterminate)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	2	5	
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Change at Week 2 (N = 59, 25, 6, 13, 4, 2, 5)	-4.23 (± 1.333)	-5.29 (± 0.269)	-3.24 (± 1.668)	
Change at Week 4 (N = 59, 25, 7, 16, 4, 2, 5)	-4.48 (± 1.547)	-5.29 (± 0.269)	-3.26 (± 1.692)	
Change at Week 6 (N = 59, 25, 7, 16, 4, 2, 5)	-4.48 (± 1.547)	-5.29 (± 0.269)	-3.26 (± 1.692)	
Change at Week 8 (N = 59, 25, 7, 16, 4, 2, 5)	-4.48 (± 1.547)	-5.29 (± 0.269)	-3.26 (± 1.692)	
Change at Week 12 (N = 59, 25, 7, 16, 4, 2, 5)	-4.48 (± 1.547)	-5.29 (± 0.269)	-3.26 (± 1.692)	

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:	
Participants in the Full Analysis Set were analyzed.	
End point type	Secondary
End point timeframe:	
Weeks 2, 4, 6, 8, and 12	

End point values	SOF/VEL	SOF/VEL (GT-1)	SOF/VEL (GT-2)	SOF/VEL (GT-3)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	59	25	7	16
Units: Percentage of participants				
number (confidence interval 95%)				
Week 2	67.8 (54.4 to 79.4)	76.0 (54.9 to 90.6)	85.7 (42.1 to 99.6)	43.8 (19.8 to 70.1)
Week 4	100.0 (93.9 to 100.0)	100.0 (86.3 to 100.0)	100.0 (59.0 to 100.0)	100.0 (79.4 to 100.0)
Week 6	100.0 (93.9 to 100.0)	100.0 (86.3 to 100.0)	100.0 (59.0 to 100.0)	100.0 (79.4 to 100.0)
Week 8	100.0 (93.9 to 100.0)	100.0 (86.3 to 100.0)	100.0 (59.0 to 100.0)	100.0 (79.4 to 100.0)
Week 12	100.0 (93.9 to 100.0)	100.0 (86.3 to 100.0)	100.0 (59.0 to 100.0)	100.0 (79.4 to 100.0)

End point values	SOF/VEL (GT-4)	SOF/VEL (GT-6)	SOF/VEL (Indeterminate)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	2	5	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 2	50.0 (6.8 to 93.2)	100.0 (15.8 to 100.0)	80.0 (28.4 to 99.5)	
Week 4	100.0 (39.8 to 100.0)	100.0 (15.8 to 100.0)	100.0 (47.8 to 100.0)	
Week 6	100.0 (39.8 to 100.0)	100.0 (15.8 to 100.0)	100.0 (47.8 to 100.0)	
Week 8	100.0 (39.8 to 100.0)	100.0 (15.8 to 100.0)	100.0 (47.8 to 100.0)	
Week 12	100.0 (39.8 to 100.0)	100.0 (15.8 to 100.0)	100.0 (47.8 to 100.0)	

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:

Participants in the Full Analysis Set were analyzed.
Virologic failure was defined as:
- On-treatment virologic failure:
-- Breakthrough (confirmed HCV RNA ≥ 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 ≥ LLOQ through 8 weeks of treatment)
- Virologic relapse:
-- Confirmed HCV RNA ≥ LLOQ during the posttreatment period having achieved HCV RNA < LLOQ at last on-treatment visit

End point type	Secondary

End point timeframe:

Baseline to Posttreatment Week 24

End point values	SOF/VEL	SOF/VEL (GT-1)	SOF/VEL (GT-2)	SOF/VEL (GT-3)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	59	25	7	16
Units: Percentage of participants				
number (not applicable)	3.4	4.0	0	6.3

End point values	SOF/VEL (GT-4)	SOF/VEL (GT-6)	SOF/VEL (Indeterminate)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	2	5	
Units: Percentage of participants				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Develop Viral Resistance (as Assessed by Presence of HCV NS5A and NS5B Genes) to SOF and VEL During Treatment and After Discontinuation of Treatment

End point title	Number of Participants Who Develop Viral Resistance (as Assessed by Presence of HCV NS5A and NS5B Genes) to SOF and VEL During Treatment and After Discontinuation of Treatment

End point description:

Baseline deep sequencing of the HCV NS5A and NS5B genes was performed for all participants. For all participants with virologic failure, deep sequencing was performed at the first time point after virologic failure if the plasma or serum sample was available and HCV RNA was > 1000 IU/mL. Participants in the Resistance Analysis Population Set included all participants in the Safety Analysis Set with a virologic outcome and at least 1 gene sequenced. All data are reported at a 15% assay cutoff.

End point type	Secondary

End point timeframe:

First dose date up to Posttreatment Week 24

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	58			
Units: Percentage of participants				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic (PK) Parameter: AUCtau of SOF

End point title	Pharmacokinetic (PK) Parameter: AUCtau of SOF

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 (all participants who took at least 1 dose of study drug and had at least 1 nonmissing postdose concentration value for the corresponding analyte in plasma) with available data were analyzed. Population PK analyses of all sparse and intensive PK data were utilized to estimate steady-state AUCtau of SOF.

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 Week 6, 8, or 12 (participants who enrolled in the optional PK substudy (N=1))

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: h*ng/mL				
arithmetic mean (standard deviation)	2381.9 (± 567.63)			

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)

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. Population PK analyses of all sparse and intensive PK data were utilized to estimate steady-state AUCtau of GS-331007 .

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 Week 6, 8, or 12 (participants who enrolled in the optional PK substudy (N=1))

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	59			
Units: h*ng/mL				
arithmetic mean (standard deviation)	230989.2 (± 81453.30)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: AUCtau of VEL

End point title	PK Parameter: AUCtau of VEL

End point description:

AUCtau is defined as the population PK derived area under the concentration verses time curve of the drug over the
dosing interval. Participants in the PK Analysis Set were analyzed. Population PK analyses of all sparse and intensive PK data were utilized to estimate steady-state AUCtau of VEL.

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 Week 6, 8, or 12 (participants who enrolled in the optional PK substudy (N=1))

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	59			
Units: h*ng/mL				
arithmetic mean (standard deviation)	4279.4 (± 2198.77)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Cmax of SOF

End point title	PK Parameter: Cmax of SOF

End point description:

Cmax is defined as the population PK derived maximum concentration of the drug. Participants in the PK Analysis set with available data were analyzed. Population PK analyses of all sparse and intensive PK data were utilized to estimate steady-state Cmax of SOF.

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 Week 6, 8, or 12 (participants who enrolled in the optional PK substudy (N=1))

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: ng/mL				
arithmetic mean (standard deviation)	1041.0 (± 176.96)			

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)

End point description:

Cmax is defined as the population PK derived maximum concentration of the drug. Participants in the PK Analysis Set were analyzed. Population PK analyses of all sparse and intensive PK data were utilized to estimate steady-state Cmax of GS-331007.

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 Week 6, 8, or 12 (participants who enrolled in the optional PK substudy (N=1))

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	59			
Units: ng/mL				
arithmetic mean (standard deviation)	9776.2 (± 3433.16)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Cmax of VEL

End point title	PK Parameter: Cmax of VEL

End point description:

Cmax is defined as the population PK derived maximum concentration of the drug. Participants in the PK Analysis Set were analyzed. Population PK analyses of all sparse and intensive PK data were utilized to estimate steady-state Cmax of VEL.

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 Week 6, 8, or 12 (participants who enrolled in the optional PK substudy (N=1))

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	59			
Units: ng/mL				
arithmetic mean (standard deviation)	226.9 (± 92.80)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Ctau of VEL

End point title	PK Parameter: Ctau of VEL

End point description:

Ctau is defined as the population PK derived concentration of the drug at the end of a 24 hour dosing interval. The 24 hour Ctau is estimated based on the combination of sparse PK samples collected at random times across the dosing interval as well as intensive PK samples collected for up to 12 hours post-dose. Participants in the PK Analysis Set were analyzed. Population PK analyses of all sparse and intensive PK data were utilized to estimate steady-state Ctau of VEL.

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 Week 6, 8, or 12 (participants who enrolled in the optional PK substudy (N=1))

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	59			
Units: ng/mL				
arithmetic mean (standard deviation)	137.2 (± 95.91)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
First dose date up to Week 12 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.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups	
Reporting group title	SOF/VEL
Reporting group description:	
SOF/VEL (400/100 mg) FDC tablet orally once daily for 12 weeks	

Serious adverse events	SOF/VEL		
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 59 (18.64%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neurilemmoma benign			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Post procedural swelling			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pubis fracture			

subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure congestive			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Depression			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Device related infection			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection viral			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Pneumonia			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Streptococcal bacteraemia			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	SOF/VEL		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 59 (55.93%)		
Nervous system disorders			
Headache			
subjects affected / exposed	10 / 59 (16.95%)		
occurrences (all)	11		
Dizziness			
subjects affected / exposed	5 / 59 (8.47%)		
occurrences (all)	5		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	8 / 59 (13.56%)		
occurrences (all)	10		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	8 / 59 (13.56%)		
occurrences (all)	9		
Vomiting			
subjects affected / exposed	8 / 59 (13.56%)		
occurrences (all)	10		
Constipation			
subjects affected / exposed	4 / 59 (6.78%)		
occurrences (all)	4		
Diarrhoea			

subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	3 / 59 (5.08%) 3 3 / 59 (5.08%) 3 3 / 59 (5.08%) 3		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	5 / 59 (8.47%) 5		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	6 / 59 (10.17%) 6		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Muscle spasms subjects affected / exposed occurrences (all)	4 / 59 (6.78%) 4 3 / 59 (5.08%) 3		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	3 / 59 (5.08%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 November 2016	• The hemodialysis PK substudy design was updated to remove dialysate collection. • An inclusion criterion that the most recent HCV treatment must have been completed at least 8 weeks prior to screening was added.
30 January 2017	• Infection with hepatitis B virus (HBV) was removed from the exclusion criteria • Hepatitis B core antibody (HBcAb) and hepatitis B surface antigen (HBsAg) testing was added at screening. In addition, for subjects who were HBcAb+ at screening, HBV DNA testing was performed at baseline/Day 1, every 4 weeks on-treatment and at posttreatment Weeks 4, 12, and 24. • During the conduct of the study, the number of subjects the Data Monitoring Committee (DMC) would evaluate was updated from the first 25 subjects to the first 12 subjects having completed 12 weeks of treatment or early termination, and every 3 months thereafter. The subsequent safety reviews alternated between a review by the DMC chair of all serious adverse events (SAEs) and deaths, and a review of safety data by the DMC meeting as specified by the DMC charter.
02 March 2017	Nonclinical toxicology information was added to communicate to investigators the potential for hematologic toxicity (decreased red blood cell [RBC] counts) associated with higher GS-331007 exposure.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported