EU Clinical Trials Register

Clinical trial results:
A Phase 1 Relative Bioavailability and Food Effect Study of a Pediatric Oral Granule Formulation of SOF/VEL in Healthy Adult Subjects

Summary

EudraCT number	2017-004044-37
Trial protocol	Outside EU/EEA
Global end of trial date	23 October 2017

Results information

Result version number	v1 (current)
This version publication date	03 November 2018
First version publication date	03 November 2018

Trial information

Trial identification

Sponsor protocol code	GS-US-342-1142

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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)	Yes
EMA paediatric investigation plan number(s)	EMEA-001646-PIP01-14
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	23 October 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 October 2017
Global end of trial reached?	Yes
Global end of trial date	23 October 2017
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 the relative bioavailability of a pediatric oral granule formulation of sofosbuvir/velpatasvir (SOF/VEL) fixed-dose combination (FDC) relative to tablet formulation and to evaluate the effect of concomitant food intake on the pharmacokinetics of a pediatric granule formulation of SOF/VEL.

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 March 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	United States: 112
Worldwide total number of subjects	112
EEA total number of subjects	0

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)	112
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 1 study site in the United States. The first participant was screened on 27 March 2017. The last study visit occurred on 23 October 2017.

Pre-assignment

Screening details:

187 participants were screened.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment AB

Arm description:

Treatment A, 8-day washout, and then Treatment B.

Arm type	Experimental
Investigational medicinal product name	Sofosbuvir/velpatasvir
Investigational medicinal product code	
Other name	Epclusa®, SOF/VEL, GS-7977/GS-5816
Pharmaceutical forms	Granules, Tablet
Routes of administration	Oral use

Dosage and administration details:

Treatment A: Single dose of SOF/VEL (400/100 mg tablet) under fasted conditions; Treatment B: Single dose of SOF/VEL (8 x 50/12.5 mg oral granules; FDC1 - 20% taste-mask coating) under fasted conditions

Arm title	Treatment BA

Arm description:

Treatment B, 8-day washout, and then Treatment A.

Arm type	Experimental
Investigational medicinal product name	Sofosbuvir/velpatasvir
Investigational medicinal product code	
Other name	Epclusa®, SOF/VEL, GS-7977/GS-5816
Pharmaceutical forms	Granules, Tablet
Routes of administration	Oral use

Dosage and administration details:

Treatment B: Single dose of SOF/VEL (8 x 50/12.5 mg oral granules; FDC1 - 20% taste-mask coating) under fasted conditions; Treatment A: Single dose of SOF/VEL (400/100 mg tablet) under fasted conditions

Arm title	Treatment ACG

Arm description:

Treatment A, 8-day washout, Treatment C, 8-day washout, and then Treatment G.

Arm type	Experimental
Investigational medicinal product name	Sofosbuvir/velpatasvir
Investigational medicinal product code	
Other name	Epclusa®, SOF/VEL, GS-7977/GS-5816
Pharmaceutical forms	Granules, Tablet
Routes of administration	Oral use

Dosage and administration details:

Treatment A: Single dose of SOF/VEL (400/100 mg tablet) under fasted conditions; Treatment C: Single dose of SOF/VEL (8 x 50/12.5 mg oral granules; FDC2 - 5% taste-mask coating) under fasted conditions; Treatment G: Single dose of SOF/VEL (8 x 50/12.5 mg oral granules; FDC2 - 5% taste-mask coating) under fed conditions

Arm title	Treatment CAG

Arm description:

Treatment C, 8-day washout, Treatment A, 8-day washout, and then Treatment G.

Arm type	Experimental
Investigational medicinal product name	Sofosbuvir/velpatasvir
Investigational medicinal product code	
Other name	Epclusa®, SOF/VEL, GS-7977/GS-5816
Pharmaceutical forms	Granules, Tablet
Routes of administration	Oral use

Dosage and administration details:

Treatment C: Single dose of SOF/VEL (8 x 50/12.5 mg oral granules; FDC2 - 5% taste-mask coating) under fasted conditions; Treatment A: Single dose of SOF/VEL (400/100 mg tablet) under fasted conditions; Treatment G: Single dose of SOF/VEL (8 x 50/12.5 mg oral granules; FDC2 - 5% taste-mask coating) under fed conditions

Number of subjects in period 1	Treatment AB	Treatment BA	Treatment ACG
Started	28	28	28
Completed	28	28	28

Number of subjects in period 1	Treatment CAG
Started	28
Completed	28

Baseline characteristics

Reporting groups

Reporting group title	Treatment AB
Reporting group description:	
Treatment A, 8-day washout, and then Treatment B.	

Reporting group title	Treatment BA
Reporting group description:	
Treatment B, 8-day washout, and then Treatment A.	

Reporting group title	Treatment ACG
Reporting group description:	
Treatment A, 8-day washout, Treatment C, 8-day washout, and then Treatment G.	

Reporting group title	Treatment CAG
Reporting group description:	
Treatment C, 8-day washout, Treatment A, 8-day washout, and then Treatment G.	

Reporting group values	Treatment AB	Treatment BA	Treatment ACG
Number of subjects	28	28	28
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	34	34	35
standard deviation	± 7.5	± 7.4	± 7.2
Gender categorical Units: Subjects			
Female	13	12	10
Male	15	16	18
Race Units: Subjects			
Black or African American	10	9	11
White	18	19	17
Ethnicity Units: Subjects			
Hispanic or Latino	21	21	23
Not Hispanic or Latino	7	7	5

Reporting group values	Treatment CAG	Total	
Number of subjects	28	112	
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	35		
standard deviation	± 7.7	-	
Gender categorical Units: Subjects			
Female	8	43	
Male	20	69	
Race Units: Subjects			
Black or African American	10	40	
White	18	72	
Ethnicity Units: Subjects			
Hispanic or Latino	19	84	
Not Hispanic or Latino	9	28	

End points

End points reporting groups

Reporting group title	Treatment AB
Reporting group description:	
Treatment A, 8-day washout, and then Treatment B.	

Reporting group title	Treatment BA
Reporting group description:	
Treatment B, 8-day washout, and then Treatment A.	

Reporting group title	Treatment ACG
Reporting group description:	
Treatment A, 8-day washout, Treatment C, 8-day washout, and then Treatment G.	

Reporting group title	Treatment CAG
Reporting group description:	
Treatment C, 8-day washout, Treatment A, 8-day washout, and then Treatment G.	

Subject analysis set title	Cohort 1, Treatment A
Subject analysis set type	Per protocol
Subject analysis set description:	
Single dose of SOF/VEL (400/100 mg tablet) under fasted conditions	

Subject analysis set title	Cohort 1, Treatment B
Subject analysis set type	Per protocol
Subject analysis set description:	
Single dose of SOF/VEL (8 x 50/12.5 mg oral granules; FDC1 - 20% taste-mask coating) under fasted conditions	

Subject analysis set title	Cohort 2, Treatment A
Subject analysis set type	Per protocol
Subject analysis set description:	
Single dose of SOF/VEL (400/100 mg tablet) under fasted conditions	

Subject analysis set title	Cohort 2, Treatment C
Subject analysis set type	Per protocol
Subject analysis set description:	
Single dose of SOF/VEL (8 x 50/12.5 mg oral granules; FDC2 - 5% taste-mask coating) under fasted conditions	

Subject analysis set title	Cohort 2, Treatment G
Subject analysis set type	Per protocol
Subject analysis set description:	
Single dose of SOF/VEL (8 x 50/12.5 mg oral granules; FDC2 - 5% taste-mask coating) under fed conditions	

Subject analysis set title	Cohorts 1 and 2, Treatment A
Subject analysis set type	Per protocol
Subject analysis set description:	
Single dose of SOF/VEL (400/100 mg tablet) under fasted conditions	

Primary: Pharmacokinetic (PK) Parameter: AUCinf of VEL, GS-331007, SOF, and GS-566500

End point title	Pharmacokinetic (PK) Parameter: AUCinf of VEL, GS-331007, SOF, and GS-566500[1]

End point description:

AUCinf is defined as the concentration of drug extrapolated to infinite time. Participants in the PK Analysis Set (all randomized participants who took at least 1 dose of study drug and had at least 1 nonmissing postdose concentration value reported for the corresponding analyte) with available data were analyzed.

End point type	Primary

End point timeframe:

Predose, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12, 16, 24, 48, 72, 96 and 120 hours postdose on Days 1 and 10 (all cohorts) and Day 19 (Cohorts 2)

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: The statistical analysis of this primary endpoint is provided in the attachment.

End point values	Cohort 1, Treatment A	Cohort 1, Treatment B	Cohort 2, Treatment A	Cohort 2, Treatment C
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	56	56	56	56[2]
Units: h*ng/mL				
arithmetic mean (standard deviation)				
VEL	4294.8 (± 1592.02)	2991.7 (± 1389.73)	4113.1 (± 2552.71)	3782.7 (± 2117.47)
GS-331007	12396.5 (± 2502.62)	11864.5 (± 2691.27)	11721.6 (± 2856.44)	11910.3 (± 2656.29)
SOF	1938.6 (± 515.08)	1287.8 (± 488.60)	1744.5 (± 946.53)	1640.4 (± 725.66)
GS-566500	2174.8 (± 482.64)	1626.1 (± 521.60)	1968.8 (± 720.73)	1917.2 (± 665.94)

Notes:

[2] - For SOF, only 54 participants were included.

End point values	Cohort 2, Treatment G			
Subject group type	Subject analysis set			
Number of subjects analysed	56			
Units: h*ng/mL				
arithmetic mean (standard deviation)				
VEL	3957.5 (± 1742.21)			
GS-331007	12341.7 (± 2707.27)			
SOF	2523.7 (± 903.08)			
GS-566500	2777.5 (± 516.80)			

Attachments (see zip file)	Statistical Comparisons/342-

Statistical analyses

No statistical analyses for this end point

Primary: PK Parameter: AUClast of VEL, GS-331007, SOF, and GS-566500

End point title	PK Parameter: AUClast of VEL, GS-331007, SOF, and GS-566500[3]

End point description:

AUClast is defined as the concentration of drug from time zero to the last observable concentration. Participants in the PK Analysis Set were analyzed.

End point type	Primary

End point timeframe:

Predose, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12, 16, 24, 48, 72, 96 and 120 hours postdose on Days 1 and 10 (all cohorts) and Day 19 (Cohorts 2)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The statistical analysis of this primary endpoint is provided in the attachment.

End point values	Cohort 1, Treatment A	Cohort 1, Treatment B	Cohort 2, Treatment A	Cohort 2, Treatment C
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	56	56	56	56
Units: h*ng/mL				
arithmetic mean (standard deviation)				
VEL	4250.9 (± 1584.23)	2951.8 (± 1378.59)	4068.8 (± 2539.06)	3740.3 (± 2111.97)
GS-331007	11822.5 (± 2487.44)	11264.0 (± 2623.87)	11077.1 (± 2841.00)	11315.9 (± 2699.62)
SOF	1924.9 (± 514.38)	1255.7 (± 458.62)	1730.4 (± 943.58)	1598.3 (± 728.94)
GS-566500	2120.5 (± 475.68)	1575.7 (± 514.86)	1912.3 (± 712.23)	1868.2 (± 661.38)

End point values	Cohort 2, Treatment G			
Subject group type	Subject analysis set			
Number of subjects analysed	56			
Units: h*ng/mL				
arithmetic mean (standard deviation)				
VEL	3906.8 (± 1717.54)			
GS-331007	11678.3 (± 2564.27)			
SOF	2494.5 (± 901.25)			
GS-566500	2719.5 (± 515.94)			

Attachments (see zip file)	Statistical Comparisons/342-

Statistical analyses

No statistical analyses for this end point

Primary: PK Parameter: Cmax of VEL, GS-331007, SOF, and GS-566500

End point title	PK Parameter: Cmax of VEL, GS-331007, SOF, and GS-

End point description:

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

End point type	Primary

End point timeframe:

Predose, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12, 16, 24, 48, 72, 96 and 120 hours postdose on Days 1 and 10 (all cohorts) and Day 19 (Cohorts 2)

Notes:

[4] - 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: The statistical analysis of this primary endpoint is provided in the attachment.

End point values	Cohort 1, Treatment A	Cohort 1, Treatment B	Cohort 2, Treatment A	Cohort 2, Treatment C
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	56	56	56	56
Units: ng/mL				
arithmetic mean (standard deviation)				
VEL	533.9 (± 194.58)	359.2 (± 144.92)	497.3 (± 287.90)	476.5 (± 247.46)
GS-331007	944.3 (± 309.05)	1105.0 (± 303.95)	910.3 (± 265.68)	988.2 (± 241.28)
SOF	1558.1 (± 500.39)	906.6 (± 394.83)	1474.6 (± 736.18)	1171.8 (± 525.01)
GS-566500	548.7 (± 121.54)	395.6 (± 123.23)	491.8 (± 192.16)	468.8 (± 166.42)

End point values	Cohort 2, Treatment G			
Subject group type	Subject analysis set			
Number of subjects analysed	56			
Units: ng/mL				
arithmetic mean (standard deviation)				
VEL	407.1 (± 133.36)			

GS-331007	621.9 (± 126.46)				
SOF	1194.1 (± 513.66)				
GS-566500	530.1 (± 112.28)				

Attachments (see zip file)	Statistical Comparisons/342-

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing Any Treatment-Emergent Adverse Event

End point title	Percentage of Participants Experiencing Any Treatment-Emergent Adverse Event

End point description:

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

End point type	Secondary

End point timeframe:

Up to Day 19 plus 30 days

End point values	Cohort 1, Treatment B	Cohort 2, Treatment C	Cohort 2, Treatment G	Cohorts 1 and 2, Treatment A
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	56	56	56	112
Units: percentage of participants				
number (not applicable)	1.8	5.4	3.6	7.1

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing Grade 3 or 4 Laboratory Abnormalities

End point title	Percentage of Participants Experiencing Grade 3 or 4 Laboratory Abnormalities

End point description:

Participants in the Safety Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Up to Day 19 plus 30 days

End point values	Cohort 1, Treatment B	Cohort 2, Treatment C	Cohort 2, Treatment G	Cohorts 1 and 2, Treatment A
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	56	56	56	112
Units: percentage of participants				
number (not applicable)				
Grade 3	1.8	1.8	1.8	2.7
Grade 4	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Palatability of SOF/VEL

End point title	Palatability of SOF/VEL

End point description:

The percentage of participants who rated the taste of each treatment as palatable are presented. Participants in the Safety Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Up to Day 19

End point values	Cohort 1, Treatment B	Cohort 2, Treatment C	Cohort 2, Treatment G	Cohorts 1 and 2, Treatment A
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	56	56	56	112[5]
Units: percentage of participants				
number (not applicable)	96.4	85.7	92.9	81.3

Notes:

[5] - Note: Data was missing for 14 participants in this group.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Tmax of VEL, GS-331007, SOF, and GS-566500

End point title	PK Parameter: Tmax of VEL, GS-331007, SOF, and GS-566500

End point description:

Tmax is defined as the time (observed time point) of Cmax. Participants in the PK Analysis Set were

analyzed.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12, 16, 24, 48, 72, 96 and 120 hours postdose on Days 1 and 10 (all cohorts) and Day 19 (Cohorts 2)

End point values	Cohort 1, Treatment A	Cohort 1, Treatment B	Cohort 2, Treatment A	Cohort 2, Treatment C
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	56	56	56	56
Units: hours				
median (inter-quartile range (Q1-Q3))				
VEL	1.00 (0.5 to 1.50)	1.50 (1.00 to 2.00)	0.77 (0.50 to 1.00)	1.00 (0.50 to 1.50)
GS-331007	3.00 (2.00 to 3.00)	3.00 (2.50 to 4.00)	3.00 (2.00 to 4.00)	2.50 (2.00 to 3.00)
SOF	1.00 (0.50 to 1.50)	1.50 (1.00 to 2.00)	0.77 (0.50 to 1.00)	1.00 (0.50 to 1.50)
GS-566500	1.50 (1.25 to 2.00)	2.00 (1.76 to 3.00)	2.00 (1.00 to 2.00)	2.00 (1.50 to 3.00)

End point values	Cohort 2, Treatment G			
Subject group type	Subject analysis set			
Number of subjects analysed	56			
Units: hours				
median (inter-quartile range (Q1-Q3))				
VEL	2.00 (1.50 to 2.00)			
GS-331007	4.00 (4.00 to 4.00)			
SOF	2.00 (1.50 to 2.00)			
GS-566500	3.00 (2.00 to 4.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Clast of VEL, GS-331007, SOF, and GS-566500

End point title	PK Parameter: Clast of VEL, GS-331007, SOF, and GS-566500

End point description:

Clast is defined as the last observable concentration of drug. Participants in the PK Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12, 16, 24, 48, 72, 96 and 120 hours postdose on Days 1 and 10 (all cohorts) and Day 19 (Cohorts 2)

End point values	Cohort 1, Treatment A	Cohort 1, Treatment B	Cohort 2, Treatment A	Cohort 2, Treatment C
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	56	56	56	56
Units: ng/mL				
arithmetic mean (standard deviation)				
VEL	1.82 (± 0.545)	1.70 (± 0.639)	1.79 (± 0.769)	1.79 (± 0.554)
GS-331007	14.27 (± 2.924)	14.35 (± 2.920)	15.52 (± 4.308)	14.68 (± 3.544)
SOF	20.64 (± 17.937)	30.78 (± 54.399)	20.87 (± 17.442)	23.33 (± 19.756)
GS-566500	18.10 (± 5.043)	16.90 (± 4.372)	18.94 (± 5.778)	16.67 (± 4.123)

End point values	Cohort 2, Treatment G			
Subject group type	Subject analysis set			
Number of subjects analysed	56			
Units: ng/mL				
arithmetic mean (standard deviation)				
VEL	1.88 (± 0.929)			
GS-331007	15.58 (± 4.071)			
SOF	32.88 (± 37.844)			
GS-566500	17.46 (± 6.649)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Tlast of VEL, GS-331007, SOF, and GS-566500

End point title	PK Parameter: Tlast of VEL, GS-331007, SOF, and GS-566500

End point description:

Tlast is defined as the time (observed time point) of Clast. Participants in the PK Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12, 16, 24, 48, 72, 96 and 120 hours postdose on Days 1 and 10

End point values	Cohort 1, Treatment A	Cohort 1, Treatment B	Cohort 2, Treatment A	Cohort 2, Treatment C
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	56	56	56	56
Units: hours				
median (inter-quartile range (Q1-Q3))				
VEL	96.00 (72.00 to 120.00)	72.00 (72.00 to 96.00)	96.00 (72.00 to 120.00)	96.00 (72.00 to 96.00)
GS-331007	96.01 (96.00 to 120.00)	96.00 (96.00 to 108.00)	96.00 (96.00 to 120.00)	96.00 (96.00 to 120.00)
SOF	4.00 (4.00 to 4.00)	4.00 (4.00 to 4.00)	4.00 (3.50 to 4.00)	4.00 (4.00 to 4.00)
GS-566500	12.00 (12.00 to 12.00)	12.00 (12.00 to 12.00)	12.00 (10.00 to 12.00)	12.00 (12.00 to 12.00)

End point values	Cohort 2, Treatment G			
Subject group type	Subject analysis set			
Number of subjects analysed	56			
Units: hours				
median (inter-quartile range (Q1-Q3))				
VEL	96.00 (72.00 to 120.00)			
GS-331007	120.00 (120.00 to 120.00)			
SOF	6.00 (5.00 to 8.00)			
GS-566500	16.00 (16.00 to 16.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: t1/2 of VEL, GS-331007, SOF, and GS-566500

End point title	PK Parameter: t1/2 of VEL, GS-331007, SOF, and GS-566500

End point description:

t1/2 is defined as the estimate of the terminal elimination half-life of the drug. Participants in the PK Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12, 16, 24, 48, 72, 96 and 120 hours postdose on Days 1 and 10 (all cohorts) and Day 19 (Cohorts 2)

End point values	Cohort 1, Treatment A	Cohort 1, Treatment B	Cohort 2, Treatment A	Cohort 2, Treatment C
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	56	56	56	56
Units: hours				
median (inter-quartile range (Q1-Q3))				
VEL	15.47 (13.58 to 19.21)	15.11 (13.14 to 17.85)	17.82 (13.11 to 19.98)	16.54 (13.31 to 19.17)
GS-331007	27.22 (25.59 to 30.04)	26.15 (24.33 to 30.15)	27.82 (24.64 to 31.79)	26.29 (23.92 to 31.25)
SOF	0.42 (0.37 to 0.47)	0.40 (0.36 to 0.45)	0.44 (0.40 to 0.49)	0.43 (0.37 to 0.48)
GS-566500	2.09 (1.99 to 2.16)	2.07 (1.90 to 2.21)	2.05 (1.97 to 2.16)	2.05 (1.92 to 2.20)

End point values	Cohort 2, Treatment G			
Subject group type	Subject analysis set			
Number of subjects analysed	56			
Units: hours				
median (inter-quartile range (Q1-Q3))				
VEL	17.52 (14.56 to 20.57)			
GS-331007	28.77 (27.00 to 31.14)			
SOF	0.58 (0.49 to 0.67)			
GS-566500	2.33 (2.19 to 2.51)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Up to Day 19 plus 30 days

Adverse event reporting additional description:

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

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Cohorts 1 and 2, Treatment A

Reporting group description:

Single dose of SOF/VEL (400/100 mg tablet) under fasted conditions

Reporting group title	Cohort 1, Treatment B

Reporting group description:

Single dose of SOF/VEL (8 x 50/12.5 mg oral granules; FDC1 - 20% taste-mask coating) under fasted conditions

Reporting group title	Cohort 2, Treatment C

Reporting group description:

Single dose of SOF/VEL (8 x 50/12.5 mg oral granules; FDC2 - 5% taste-mask coating) under fasted conditions

Reporting group title	Cohort 2, Treatment G

Reporting group description:

Single dose of SOF/VEL (8 x 50/12.5 mg oral granules; FDC2 - 5% taste-mask coating) under fed conditions

Serious adverse events	Cohorts 1 and 2, Treatment A	Cohort 1, Treatment B	Cohort 2, Treatment C
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 112 (0.00%)	0 / 56 (0.00%)	0 / 56 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Cohort 2, Treatment G		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 56 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Cohorts 1 and 2, Treatment A	Cohort 1, Treatment B	Cohort 2, Treatment C
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 112 (0.00%)	0 / 56 (0.00%)	0 / 56 (0.00%)

Non-serious adverse events	Cohort 2, Treatment G		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 56 (0.00%)		

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: None of the treatment-emergent nonserious AEs occurred in at least 5% of participants of any of the treatment arms.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

 None reported