Clinical trial results:
A Phase 3, Open-label Study to Investigate the Efficacy and Safety of Sofosbuvir/Velpatasvir Fixed Dose Combination for 12 weeks in Subjects with Chronic Hepatitis C Virus (HCV) infection

Summary

EudraCT number	2015-003001-42
Trial protocol	SE
Global end of trial date	13 September 2017

Results information

Result version number	v1 (current)
This version publication date	02 August 2018
First version publication date	02 August 2018

Trial information

Trial identification

Sponsor protocol code	GS-US-342-1522

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02722837
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	13 September 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 June 2017
Global end of trial reached?	Yes
Global end of trial date	13 September 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the efficacy, safety, and tolerability of treatment with sofosbuvir/velpatasvir (SOF/VEL) fixed-dose combination (FDC) for 12 weeks in participants with chronic hepatitis C virus (HCV) infection.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.
This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 April 2016
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	Russian Federation: 103
Country: Number of subjects enrolled	Sweden: 16
Worldwide total number of subjects	119
EEA total number of subjects	16

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)	116
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in the Russian Federation and Sweden. The first participant was screened on 04 April 2016 and the last study visit occurred on 13 September 2017.

Pre-assignment

Screening details:

122 participants were screened.

Period 1

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

Arms

Arm title	SOF/VEL

Arm description:

SOF/VEL for 12 weeks

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

Dosage and administration details:

400/100 mg fixed-dose combination (FDC) tablet administered orally once daily for 12 weeks, with or without food

Number of subjects in period 1	SOF/VEL
Started	119
Completed	119

Baseline characteristics

Reporting groups	
Reporting group title	SOF/VEL
Reporting group description:	
SOF/VEL for 12 weeks	

Reporting group values	SOF/VEL	Total	
Number of subjects	119	119	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	44		
standard deviation	± 11.1	-	
Gender categorical Units: Subjects			
Female	59	59	
Male	60	60	
Race Units: Subjects			
Asian	2	2	
White	117	117	
Ethnicity Units: Subjects			
Not Hispanic or Latino	119	119	
IL28b Status			
The CC, CT, and TT alleles are different forms of the IL28b gene.			
Units: Subjects			
CC	29	29	
CT	72	72	
TT	18	18	
HCV RNA Units: Subjects			
< 800,000 IU/mL	38	38	
≥ 800,000 IU/mL	81	81	
HCV RNA Units: log10 IU/mL			
arithmetic mean	6.1		
standard deviation	± 0.54	-	

End points

End points reporting groups

Reporting group title	SOF/VEL
Reporting group description:	
SOF/VEL for 12 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 HCV RNA < the lower limit of quantitation (LLOQ) at 12 weeks after stopping study treatment. Participants in the Full Analysis Set (participants who received at least 1 dose of study drug) were analyzed.	
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 analysis was planned or performed.

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	119			
Units: percentage of participants				
number (confidence interval 95%)	99.2 (95.4 to 100.0)			

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]
End point description:	
Participants in the Safety Analysis Set (all participants who received at least one dose of the study drug) were analyzed.	
End point type	Primary
End point timeframe:	
Up to 12 weeks	

Notes:

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

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	119			
Units: percentage of participants				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HCV RNA < LLOQ at 4 Weeks After Discontinuation of Therapy (SVR4)

End point title	Percentage of Participants With HCV RNA < LLOQ at 4 Weeks After Discontinuation of Therapy (SVR4)

End point description:

SVR4 was defined as HCV RNA < LLOQ at 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			
Subject group type	Reporting group			
Number of subjects analysed	119			
Units: percentage of participants				
number (confidence interval 95%)	100.0 (96.6 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HCV RNA < LLOQ at 24 Weeks After Discontinuation of Therapy (SVR24)

End point title	Percentage of Participants With HCV RNA < LLOQ at 24 Weeks After Discontinuation of Therapy (SVR24)

End point description:

SVR24 was defined as HCV RNA < LLOQ at 24 weeks after stopping study treatment.

End point type	Secondary

End point timeframe:

Posttreatment Week 24

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	119			
Units: percentage of participants				
number (confidence interval 95%)	99.2 (95.4 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HCV RNA < LLOQ on Treatment at Week 1

End point title	Percentage of Participants With HCV RNA < LLOQ on Treatment at Week 1
End point description:	
Participants in the Full Analysis Set were analyzed.	
End point type	Secondary
End point timeframe:	
Week 1	

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	119			
Units: percentage of participants				
number (confidence interval 95%)	21.0 (14.1 to 29.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HCV RNA < LLOQ on Treatment at Week 2

End point title	Percentage of Participants With HCV RNA < LLOQ on Treatment at Week 2
End point description:	
Participants in the Full Analysis Set were analyzed.	
End point type	Secondary
End point timeframe:	
Week 2	

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	119			
Units: percentage of participants				
number (confidence interval 95%)	64.7 (55.4 to 73.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HCV RNA < LLOQ on Treatment at Week 4

End point title	Percentage of Participants With HCV RNA < LLOQ on Treatment at Week 4
End point description:	
Participants in the Full Analysis Set were analyzed.	
End point type	Secondary
End point timeframe:	
Week 4	

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	119			
Units: percentage of participants				
number (confidence interval 95%)	96.6 (91.6 to 99.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HCV RNA < LLOQ on Treatment at Week 8

End point title	Percentage of Participants With HCV RNA < LLOQ on Treatment at Week 8
End point description:	
Participants in the Full Analysis Set were analyzed.	
End point type	Secondary
End point timeframe:	
Week 8	

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	119			
Units: percentage of participants				
number (confidence interval 95%)	100.0 (96.9 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HCV RNA < LLOQ on Treatment at Week 12

End point title	Percentage of Participants With HCV RNA < LLOQ on Treatment at Week 12
End point description:	
Participants in the Full Analysis Set were analyzed.	
End point type	Secondary
End point timeframe:	
Week 12	

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	119			
Units: percentage of participants				
number (confidence interval 95%)	100.0 (96.9 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in HCV RNA at Week 1

End point title	Change From Baseline in HCV RNA at Week 1
End point description:	
Participants in the Full Analysis Set with available data were analyzed.	
End point type	Secondary
End point timeframe:	
Baseline (Day 1); Week 1	

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	118			
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-4.17 (± 0.502)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in HCV RNA at Week 2

End point title	Change From Baseline in HCV RNA at Week 2
End point description:	
Participants in the Full Analysis Set with available data were analyzed.	
End point type	Secondary
End point timeframe:	
Baseline (Day 1); Week 2	

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	117			
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-4.70 (± 0.525)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in HCV RNA at Week 4

End point title	Change From Baseline in HCV RNA at Week 4
End point description:	
Participants in the Full Analysis Set were analyzed.	
End point type	Secondary
End point timeframe:	
Baseline (Day 1); Week 4	

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	119			
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-4.90 (± 0.540)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in HCV RNA at Week 8

End point title	Change From Baseline in HCV RNA at Week 8
End point description:	
Participants in the Full Analysis Set were analyzed.	
End point type	Secondary
End point timeframe:	
Baseline (Day 1); Week 8	

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	119			
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-4.93 (± 0.544)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in HCV RNA at Week 12

End point title	Change From Baseline in HCV RNA at Week 12
End point description:	
Participants in the Full Analysis Set were analyzed.	
End point type	Secondary
End point timeframe:	
Baseline (Day 1); Week 12	

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	119			
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-4.93 (± 0.544)			

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:

Virologic failure was defined as:
• 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), or
• Relapse (HCV RNA ≥ LLOQ during the post-treatment period having achieved HCV RNA < LLOQ at end of
treatment, confirmed with 2 consecutive values or last available post-treatment measurement)
Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Up to Posttreatment Week 24

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	119			
Units: percentage of participants				
number (not applicable)	0.8			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 12 weeks + 30 days	
Adverse event reporting additional description:	
Safety Analysis Set	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups	
Reporting group title	SOF/VEL
Reporting group description:	
SOF/VEL (400/100 mg) FDC tablet administered orally once daily for 12 weeks, with or without food	

Serious adverse events	SOF/VEL		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 119 (3.36%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Spinal compression fracture			
subjects affected / exposed	1 / 119 (0.84%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Sciatica			
subjects affected / exposed	1 / 119 (0.84%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	1 / 119 (0.84%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Orchitis			

subjects affected / exposed	1 / 119 (0.84%)		
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	29 / 119 (24.37%)		
Nervous system disorders			
Headache			
subjects affected / exposed	19 / 119 (15.97%)		
occurrences (all)	28		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	8 / 119 (6.72%)		
occurrences (all)	8		
Asthenia			
subjects affected / exposed	7 / 119 (5.88%)		
occurrences (all)	7		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 December 2015	Updated the referenced version of the Declaration of Helsinki Specified need for local competent authority review and approval of substantial protocol modifications prior to implementation

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported