Clinical trial results:
An Open Label Study of Sofosbuvir/GS-5816 Fixed-Dose Combination in Subjects with Chronic HCV Infection

Summary

EudraCT number	2014-003898-42
Trial protocol	GB DE BE IT
Global end of trial date	15 June 2016

Results information

Result version number	v1 (current)
This version publication date	18 May 2017
First version publication date	18 May 2017

Trial information

Trial identification

Sponsor protocol code	GS-US-342-1446

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02346721
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	15 June 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 June 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study were to evaluate the efficacy, safety, and tolerability of treatment with sofosbuvir/velpatasvir (SOF/VEL) in participants with chronic genotype 1, 2, 4, 6 or indeterminate HCV infection who received placebo in the Gilead-sponsored study GS-US-342-1138.

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	23 February 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	China: 1
Country: Number of subjects enrolled	Hong Kong: 3
Country: Number of subjects enrolled	Puerto Rico: 2
Country: Number of subjects enrolled	United States: 42
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	France: 31
Country: Number of subjects enrolled	United Kingdom: 13
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Italy: 2
Worldwide total number of subjects	111
EEA total number of subjects	57

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)	100
From 65 to 84 years	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in North America, Europe, and Asia Pacific. The first participant was screened on 23 February 2015. The last study visit occurred on 15 June 2016.

Pre-assignment

Screening details:

116 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 12 Weeks

Arm description:

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

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

Dosage and administration details:

400/100 mg administered once daily

Number of subjects in period 1	SOF/VEL 12 Weeks
Started	111
Completed	107
Not completed	4
Withdrew Consent	3
Lack of Efficacy	1

Baseline characteristics

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

Reporting group values	SOF/VEL 12 Weeks	Total	
Number of subjects	111	111	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	54		
standard deviation	± 10.4	-	
Gender categorical Units: Subjects			
Female	46	46	
Male	65	65	
Race Units: Subjects			
Black or African American	12	12	
White	85	85	
Asian	11	11	
Native Hawaiian or Pacific Islander	1	1	
Other	2	2	
Ethinicity Units: Subjects			
Hispanic or Latino	5	5	
Not Hispanic or Latino	106	106	
IL28b Status			
The CC, CT, and TT alleles are different forms of the IL28b gene.			
Units: Subjects			
CC	36	36	
CT	50	50	
TT	25	25	
HCV RNA Category Units: Subjects			
< 800,000 IU/mL	30	30	
≥ 800,000 IU/mL	81	81	
HCV RNA Units: log10 IU/mL			
arithmetic mean	6.3		
standard deviation	± 0.55	-	

End points

End points reporting groups

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

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) 12 weeks following the last dose of study drug. Full Analysis Set (FAS) included all enrolled participants who took 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 analysis was planned or performed.

End point values	SOF/VEL 12 Weeks			
Subject group type	Reporting group			
Number of subjects analysed	111			
Units: percentage of participants				
number (confidence interval 95%)	97.3 (92.3 to 99.4)			

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Participants Who Permanently Discontinued Any Study Drug Due to an Adverse Event[2]
End point description:	
Safety Analysis Set included participants who took at least 1 dose of study drug.	
End point type	Primary
End point timeframe:	
Up to 12 weeks	

Notes:

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

End point values	SOF/VEL 12 Weeks			
Subject group type	Reporting group			
Number of subjects analysed	111			
Units: percentage of participants				
number (not applicable)	0.9			

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

Posttreatment Weeks 4 and 24

End point values	SOF/VEL 12 Weeks			
Subject group type	Reporting group			
Number of subjects analysed	111			
Units: percentage of participants				
number (confidence interval 95%)				
SVR4	98.2 (93.6 to 99.8)			
SVR24	97.3 (92.3 to 99.4)			

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Participants With HCV RNA < LLOQ While on Treatment

End point description:

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

End point type	Secondary

End point timeframe:

Baseline to Week 12

End point values	SOF/VEL 12 Weeks			
Subject group type	Reporting group			
Number of subjects analysed	111			
Units: percentage of participants				
number (confidence interval 95%)				
Week 1	18 (11.4 to 26.4)			
Week 2	55 (45.2 to 64.4)			
Week 4	94.6 (88.6 to 98)			
Week 6	99.1 (95.1 to 100)			
Week 8	100 (96.7 to 100)			
Week 10	100 (96.7 to 100)			
Week 12 (N = 110)	100 (96.7 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: HCV RNA Change From Baseline

End point title	HCV RNA Change From Baseline
End point description:	
Participants in the Full Analysis Set with available data were analyzed.	
End point type	Secondary
End point timeframe:	
Baseline to Week 12	

End point values	SOF/VEL 12 Weeks			
Subject group type	Reporting group			
Number of subjects analysed	111			
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Change at Week 1 (N= 110)	-4.23 (± 0.592)			
Change at Week 2	-4.79 (± 0.627)			
Change at Week 4	-5.1 (± 0.546)			
Change at Week 6	-5.11 (± 0.552)			

Change at Week 8	-5.11 (± 0.554)			
Change at Week 10	-5.11 (± 0.554)			
Change at Week 12 (N=110)	-5.11 (± 0.556)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Virologic Failure

End point title	Percentage of Participants With Virologic Failure

End point description:

1) 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

2) Full Analysis Set

End point type	Secondary

End point timeframe:

Up to Posttreatment Week 24

End point values	SOF/VEL 12 Weeks			
Subject group type	Reporting group			
Number of subjects analysed	111			
Units: percentage of participants				
number (not applicable)	0.9			

Statistical analyses

No statistical analyses for this end point

Adverse events

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

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0

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

Serious adverse events	SOF/VEL 12 Weeks		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 111 (4.50%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gallbladder adenocarcinoma			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatocellular carcinoma			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Lower limb fracture			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Meniscus injury			

subjects affected / exposed	1 / 111 (0.90%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 111 (0.90%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lymphangitis			
subjects affected / exposed	1 / 111 (0.90%)		
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 12 Weeks		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	46 / 111 (41.44%)		
Nervous system disorders			
Headache			
subjects affected / exposed	24 / 111 (21.62%)		
occurrences (all)	32		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	18 / 111 (16.22%)		
occurrences (all)	18		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	7 / 111 (6.31%)		
occurrences (all)	7		
Nausea			
subjects affected / exposed	12 / 111 (10.81%)		
occurrences (all)	12		
Respiratory, thoracic and mediastinal disorders			

Cough subjects affected / exposed occurrences (all)	7 / 111 (6.31%) 8		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 April 2015	Update to concomitant medications to prohibit the use of amiodarone from 60 days prior to Baseline/Day 1 through the end of treatment due to new safety information

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported