



Clinical trial results:

A Phase 2, Multicenter, Open-Label Study to Evaluate the Efficacy and Safety of Sofosbuvir/Velpatasvir Fixed Dose Combination in Subjects with Chronic HCV Infection who have Received a Liver Transplant Summary

EudraCT number	2016-000416-15
Trial protocol	GB
Global end of trial date	28 July 2017

Results information

Result version number	v1 (current)
This version publication date	10 August 2018
First version publication date	10 August 2018

Trial information

Trial identification

Sponsor protocol code	GS-US-342-2104
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02781571
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	28 July 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 July 2017
Global end of trial reached?	Yes
Global end of trial date	28 July 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 efficacy, safety, and tolerability of sofosbuvir /velpatasvir (SOF/VEL) fixed-dose combination (FDC) in participants with chronic hepatitis C virus (HCV) who have received a liver transplant.

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 July 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	Spain: 31
Country: Number of subjects enrolled	United Kingdom: 41
Country: Number of subjects enrolled	Switzerland: 7
Worldwide total number of subjects	79
EEA total number of subjects	72

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)	47
From 65 to 84 years	32
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Spain, Switzerland, and the United Kingdom. The first participant was screened on 27 July 2016. The last study visit occurred on 28 July 2017.

Pre-assignment

Screening details:

85 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
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Arm description:

SOF/VEL in participants with chronic HCV infection who received a liver transplant

Arm type	Experimental
Investigational medicinal product name	Sofosbuvir/Velpatasvir
Investigational medicinal product code	
Other name	SOF/VEL; Epclusa®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

400/100 mg FDC once daily for 12 weeks

Number of subjects in period 1	SOF/VEL
Started	79
Completed	79

Baseline characteristics

Reporting groups

Reporting group title	Overall Study
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Reporting group description:

Safety Analysis Set: participants who took at least 1 dose of the study drug.

Reporting group values	Overall Study	Total	
Number of subjects	79	79	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	62 ± 8.7	-	
Gender categorical Units: Subjects			
Female	15	15	
Male	64	64	
Race Units: Subjects			
Black or African American	2	2	
White	65	65	
Asian	12	12	
Ethnicity Units: Subjects			
Hispanic or Latino	2	2	
Not Hispanic or Latino	77	77	
IL28b Status			
The CC, CT, and TT alleles are different forms of the IL28b gene.			
Units: Subjects			
CC	39	39	
CT	34	34	
TT	6	6	
HCV Genotype Units: Subjects			
Genotype 1	37	37	
Genotype 2	3	3	
Genotype 3	35	35	
Genotype 4	4	4	
HCV RNA Category Units: Subjects			
< 800,000 IU/mL	18	18	
≥ 800,000 IU/mL	61	61	

HCV RNA			
Units: log10 IU/mL			
arithmetic mean	6.4		
standard deviation	± 0.55	-	

End points

End points reporting groups

Reporting group title	SOF/VEL
Reporting group description: SOF/VEL in participants with chronic HCV infection who received a liver transplant	

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

End point title	Percentage of Participants With Sustained Virologic Response (SVR) 12 Weeks After Cessation of Therapy (SVR12) ^[1]
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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 (all enrolled participants who took at least 1 dose of the study drug) were analyzed.

End point type	Primary
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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			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: percentage of participants				
number (confidence interval 95%)	96.2 (89.3 to 99.2)			

Statistical analyses

No statistical analyses for this end point

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

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

Safety Analysis Set: participants who took at least 1 dose of the study drug.

End point type	Primary
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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 comparison was planned or performed.

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: percentage of participants				
number (not applicable)	1.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Sustained Virologic Response 4 Weeks After Cessation of Therapy (SVR4)

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

Posttreatment Week 4

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: percentage of participants				
number (confidence interval 95%)	97.5 (91.2 to 99.7)			

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Participants With HCV RNA < LLOQ at Week 2
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End point description:

Participants in the Full Analysis Set were analyzed.

End point type	Secondary
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End point timeframe:

Week 2

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: Percentage of participants				
number (confidence interval 95%)	40.5 (29.6 to 52.1)			

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Participants With HCV RNA < LLOQ at Week 4
End point description:	Participants in the Full Analysis Set with available data 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	78			
Units: percentage of participants				
number (confidence interval 95%)	85.9 (76.2 to 92.7)			

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Participants With HCV RNA < LLOQ at Week 8
End point description:	Participants in the Full Analysis Set with available data 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	78			
Units: percentage of participants				
number (confidence interval 95%)	98.7 (93.1 to 100.0)			

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Participants With HCV RNA < LLOQ at Week 12
End point description:	Participants in the Full Analysis Set with available data 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	78			
Units: percentage of participants				
number (confidence interval 95%)	100.0 (95.4 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: HCV RNA at Week 2

End point title	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:	Week 2

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	75			
Units: log10 IU/mL				
arithmetic mean (standard deviation)	1.59 (± 0.596)			

Statistical analyses

No statistical analyses for this end point

Secondary: HCV RNA at Week 4

End point title	HCV RNA at Week 4
End point description:	Participants in the Full Analysis Set with available data 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	78			
Units: log10 IU/mL				
arithmetic mean (standard deviation)	1.23 (± 0.251)			

Statistical analyses

No statistical analyses for this end point

Secondary: HCV RNA at Week 8

End point title	HCV RNA at Week 8
End point description:	Participants in the Full Analysis Set with available data 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	77			
Units: log10 IU/mL				
arithmetic mean (standard deviation)	1.15 (± 0.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: HCV RNA at Week 12

End point title	HCV RNA at Week 12
End point description:	Participants in the Full Analysis Set with available data 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	78			
Units: log10 IU/mL				
arithmetic mean (standard deviation)	1.15 (± 0.00)			

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; Week 2

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	75			
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-4.75 (± 0.635)			

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 with available data were analyzed.	
End point type	Secondary
End point timeframe: Baseline; Week 4	

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	78			
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-5.13 (± 0.551)			

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 with available data were analyzed.	
End point type	Secondary
End point timeframe: Baseline; Week 8	

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	77			
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-5.20 (± 0.548)			

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 with available data were analyzed.	
End point type	Secondary
End point timeframe: Baseline; Week 12	

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	78			
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-5.22 (± 0.554)			

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 • On-treatment virologic failure: Breakthrough (confirmed HCV RNA ≥ LLOQ after having previously had HCV RNA < LLOQ on 2 consecutive measurements 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 12 weeks of treatment) • Virologic 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 12

End point values	SOF/VEL			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: Percentage of Participants				
number (not applicable)	2.5			

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: participants who took at least 1 dose of the study drug.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20
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Reporting groups

Reporting group title	SOF/VEL
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Reporting group description:

SOF/VEL in participants with chronic HCV infection who received a liver transplant

Serious adverse events	SOF/VEL		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 79 (3.80%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatocellular carcinoma			
subjects affected / exposed	1 / 79 (1.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Joint swelling			
subjects affected / exposed	1 / 79 (1.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia klebsiella			
subjects affected / exposed	1 / 79 (1.27%)		
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	42 / 79 (53.16%)		
Nervous system disorders			
Headache			
subjects affected / exposed	19 / 79 (24.05%)		
occurrences (all)	19		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	16 / 79 (20.25%)		
occurrences (all)	16		
Asthenia			
subjects affected / exposed	5 / 79 (6.33%)		
occurrences (all)	5		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	6 / 79 (7.59%)		
occurrences (all)	6		
Nausea			
subjects affected / exposed	6 / 79 (7.59%)		
occurrences (all)	6		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	8 / 79 (10.13%)		
occurrences (all)	8		
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	4 / 79 (5.06%)		
occurrences (all)	5		
Infections and infestations			
Influenza			
subjects affected / exposed	5 / 79 (6.33%)		
occurrences (all)	6		
Viral upper respiratory tract infection			

subjects affected / exposed occurrences (all)	5 / 79 (6.33%) 5		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	4 / 79 (5.06%) 4		

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