



Clinical trial results:

An Open-Label Study to Evaluate the Safety And Efficacy of Sofosbuvir/Velpatasvir/Voxilaprevir Fixed-Dose Combination for 12 Weeks in Subjects who Participated in a Prior Gilead-Sponsored HCV Treatment Study

Summary

EudraCT number	2017-000179-98
Trial protocol	GB
Global end of trial date	19 March 2018

Results information

Result version number	v1 (current)
This version publication date	24 March 2019
First version publication date	24 March 2019

Trial information

Trial identification

Sponsor protocol code	GS-US-367-4181
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03118843
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	19 March 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 March 2018
Global end of trial reached?	Yes
Global end of trial date	19 March 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study are to determine the efficacy, safety, and tolerability of treatment with sofosbuvir/velpatasvir/voxilaprevir (SOF/VEL/VOX) fixed-dose combination (FDC) for 12 weeks in participants with chronic hepatitis C virus (HCV) infection with or without cirrhosis, who did not achieve sustained viral response (SVR) after receiving prior treatment in a Gilead-sponsored HCV treatment study of direct-acting antiviral (DAA)-containing regimens.

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	25 April 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 Kingdom: 1
Country: Number of subjects enrolled	New Zealand: 3
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	United States: 20
Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 2
Worldwide total number of subjects	31
EEA total number of subjects	4

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)	25
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in North America, Europe, New Zealand, and Australia. The first participant was screened on 25 April 2017. The last study visit occurred on 19 March 2018.

Pre-assignment

Screening details:

38 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/VOX
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Arm description:

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

Arm type	Experimental
Investigational medicinal product name	Sofosbuvir/velpatasvir/voxilaprevir
Investigational medicinal product code	
Other name	SOF/VEL/VOX, Vosevi®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

400/100/100 mg FDC tablet administered orally once daily with food

Number of subjects in period 1	SOF/VEL/VOX
Started	31
Completed	31

Baseline characteristics

Reporting groups

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

Reporting group values	SOF/VEL/VOX	Total	
Number of subjects	31	31	
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	60		
standard deviation	± 7.1	-	
Gender categorical			
Units: Subjects			
Female	8	8	
Male	23	23	
Ethnicity			
Units: Subjects			
Hispanic or Latino	2	2	
Not Hispanic or Latino	29	29	
Race			
Units: Subjects			
White	25	25	
Black or African American	5	5	
Not Disclosed	1	1	
HCV Genotype			
Units: Subjects			
Genotype 1	19	19	
Genotype 2	2	2	
Genotype 3	8	8	
Genotype 4	1	1	
Genotype 5	1	1	
IL28b Status			
The CC, CT, and TT alleles are different forms of the IL28b gene.			
Units: Subjects			
CC	3	3	
CT	21	21	
TT	7	7	
Cirrhosis Status			
Units: Subjects			
Yes	15	15	
No	16	16	
HCV RNA Category			
Units: Subjects			

< 800,000 IU/mL	6	6	
≥ 800,000 IU/mL	25	25	

HCV RNA (log10 IU/mL)			
Units: log10 IU/mL			
arithmetic mean	6.5		
standard deviation	± 0.56	-	

End points

End points reporting groups

Reporting group title	SOF/VEL/VOX
Reporting group description: SOF/VEL/VOX (400/100/100 mg) FDC tablet once daily 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]
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End point description:

SVR12 was defined as HCV RNA < the lower limit of quantitation (LLOQ; ie, 15 IU/mL) at 12 weeks after stopping study treatment. Full Analysis Set included all enrolled participants who took at least 1 dose of study drug.

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/VOX			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: percentage of participants				
number (confidence interval 95%)	100.0 (88.8 to 100.0)			

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]
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End point description:

Participants in the Safety Analysis Set were analyzed.

End point type	Primary
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End point timeframe:

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/VOX			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: percentage of participants				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With SVR at 4 Weeks After Discontinuation of Therapy (SVR4)

End point title	Percentage of Participants With SVR at 4 Weeks After Discontinuation 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/VOX			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: percentage of participants				
number (confidence interval 95%)	100.0 (88.8 to 100.0)			

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
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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:

Weeks 2, 4, 8, and 12

End point values	SOF/VEL/VOX			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: percentage of participants				
number (confidence interval 95%)				
Week 2	51.6 (33.1 to 69.8)			
Week 4	96.8 (83.3 to 99.9)			
Week 8	100.0 (88.8 to 100.0)			
Week 12	100.0 (88.8 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:	
Virologic failure was defined as:	
1) On-treatment virologic failure:	
• Breakthrough (confirmed HCV RNA $\geq$ LLOQ after 2 consecutive HCV RNA $<$ LLOQ), or • Rebound (confirmed > 1 log₁₀ IU/mL increase in HCV RNA from nadir while on treatment), or • Non-response (HCV RNA persistently $\geq$ LLOQ through 8 weeks of treatment)	
2) Virologic relapse: Confirmed HCV RNA $\geq$ LLOQ during the posttreatment period having achieved HCV RNA $<$ LLOQ at last on-treatment visit.	
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/VOX			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: percentage of participants				
number (not applicable)	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
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End point description:

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

End point type	Secondary
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End point timeframe:

Baseline; Weeks 2, 4, 8, and 12

End point values	SOF/VEL/VOX			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Change at Week 2 (N = 29)	-5.16 (± 0.560)			
Change at Week 4 (N = 30)	-5.34 (± 0.571)			
Change at Week 8 (N = 31)	-5.34 (± 0.563)			
Change at Week 12 (N = 31)	-5.34 (± 0.563)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events: Up to 12 weeks plus 30 days; All-Cause Mortality: Up to Posttreatment Week 12

Adverse event reporting additional description:

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

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.1
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Reporting groups

Reporting group title	SOF/VEL/VOX
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Reporting group description:

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

Serious adverse events	SOF/VEL/VOX		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 31 (3.23%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 31 (3.23%)		
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/VOX		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 31 (54.84%)		

Nervous system disorders Headache subjects affected / exposed occurrences (all)	4 / 31 (12.90%) 4		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Pain subjects affected / exposed occurrences (all)	5 / 31 (16.13%) 5 2 / 31 (6.45%) 2		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Abdominal distension subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all)	5 / 31 (16.13%) 5 2 / 31 (6.45%) 2 2 / 31 (6.45%) 2 2 / 31 (6.45%) 2 2 / 31 (6.45%) 2		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 2		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) Insomnia	2 / 31 (6.45%) 2		

subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 2		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	3 / 31 (9.68%)		
occurrences (all)	3		
Pneumonia			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences (all)	2		

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