



Clinical trial results:

A Phase 3, Open-label Study to Investigate the Efficacy and Safety of Sofosbuvir plus Ribavirin in Chronic Genotype 1, 2, 3 and 4 Hepatitis C Virus (HCV) and Human Immunodeficiency Virus (HIV) Co-infected Subjects

Summary

EudraCT number	2012-004154-28
Trial protocol	GB DE IT ES
Global end of trial date	10 July 2014

Results information

Result version number	v1 (current)
This version publication date	22 March 2016
First version publication date	06 August 2015

Trial information

Trial identification

Sponsor protocol code	GS-US-334-0124
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01783678
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	10 July 2014
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	10 July 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is an Open-label Phase 3 study in adults with chronic genotypes 1, 2, 3, and 4 HCV infection who are co-infected with HIV-1.

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	18 January 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects**Subjects enrolled per country**

Country: Number of subjects enrolled	Spain: 57
Country: Number of subjects enrolled	United Kingdom: 47
Country: Number of subjects enrolled	Germany: 48
Country: Number of subjects enrolled	Italy: 49
Country: Number of subjects enrolled	Australia: 38
Country: Number of subjects enrolled	France: 36
Worldwide total number of subjects	275
EEA total number of subjects	237

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)	269
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at a total of 39 study sites in Australia and Europe. The first participant was screened on 18 January 2013. The last study visit occurred on 10 July 2014.

Pre-assignment

Screening details:

346 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

Are arms mutually exclusive?	Yes
Arm title	Genotype 2 Treatment-naive

Arm description:

Sofosbuvir (SOF) + ribavirin (RBV) for 12 weeks in treatment-naive participants with HIV-1 and genotype 2 HCV coinfection

Arm type	Experimental
Investigational medicinal product name	Sofosbuvir
Investigational medicinal product code	
Other name	Sovaldi®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

400 mg tablet administered orally once daily

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg tablets administered orally in a divided daily dose according to package insert weight-based dosing recommendations (< 75kg = 1000 mg and ≥ 75 kg = 1200 mg)

Arm title	Genotype 1 Treatment-naive
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Arm description:

SOF + RBV for 24 weeks in treatment-naive participants with HIV-1 and genotype 1 HCV coinfection

Arm type	Experimental
Investigational medicinal product name	Sofosbuvir
Investigational medicinal product code	
Other name	Sovaldi®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

400 mg tablet administered orally once daily

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
200 mg tablets administered orally in a divided daily dose according to package insert weight-based dosing recommendations (< 75kg = 1000 mg and ≥ 75 kg = 1200 mg)	
Arm title	Genotype 2 Treatment-experienced
Arm description:	
SOF + RBV for 24 weeks in treatment-experienced participants with HIV-1 and genotype 2 HCV coinfection	
Arm type	Experimental
Investigational medicinal product name	Sofosbuvir
Investigational medicinal product code	
Other name	Sovaldi®
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
400 mg tablet administered orally once daily	
Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
200 mg tablets administered orally in a divided daily dose according to package insert weight-based dosing recommendations (< 75kg = 1000 mg and ≥ 75 kg = 1200 mg)	
Arm title	Genotype 3 Treatment-naïve
Arm description:	
SOF + RBV for 24 weeks in treatment-naïve participants with HIV-1 and genotype 3 HCV coinfection	
Arm type	Experimental
Investigational medicinal product name	Sofosbuvir
Investigational medicinal product code	
Other name	Sovaldi®
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
400 mg tablet administered orally once daily	
Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
200 mg tablets administered orally in a divided daily dose according to package insert weight-based dosing recommendations (< 75kg = 1000 mg and ≥ 75 kg = 1200 mg)	
Arm title	Genotype 3 Treatment-experienced
Arm description:	
SOF + RBV for 24 weeks in treatment-experienced participants with HIV-1 and genotype 3 HCV coinfection	
Arm type	Experimental

Investigational medicinal product name	Sofosbuvir
Investigational medicinal product code	
Other name	Sovaldi®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

400 mg tablet administered orally once daily

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg tablets administered orally in a divided daily dose according to package insert weight-based dosing recommendations (< 75kg = 1000 mg and ≥ 75 kg = 1200 mg)

Arm title	Genotype 4 Treatment-naïve
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Arm description:

SOF + RBV for 24 weeks in treatment-naïve participants with HIV-1 and genotype 4 HCV coinfection

Arm type	Experimental
Investigational medicinal product name	Sofosbuvir
Investigational medicinal product code	
Other name	Sovaldi®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

400 mg tablet administered orally once daily

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg tablets administered orally in a divided daily dose according to package insert weight-based dosing recommendations (< 75kg = 1000 mg and ≥ 75 kg = 1200 mg)

Number of subjects in period 1 ^[1]	Genotype 2 Treatment-naïve	Genotype 1 Treatment-naïve	Genotype 2 Treatment- experienced
Started	19	112	6
Completed	17	94	5
Not completed	2	18	1
Withdrew Consent	1	1	-
Lost to follow-up	-	4	-
Lack of efficacy	1	13	1

Number of subjects in period 1 ^[1]	Genotype 3 Treatment-naïve	Genotype 3 Treatment- experienced	Genotype 4 Treatment-naïve
Started	57	49	31

Completed	50	42	26
Not completed	7	7	5
Withdrew Consent	2	-	-
Lost to follow-up	2	1	-
Lack of efficacy	3	6	5

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: One participant who was enrolled but not treated is not included in the subject disposition table.

Baseline characteristics

Reporting groups

Reporting group title	Genotype 2 Treatment-naïve
Reporting group description: Sofosbuvir (SOF) + ribavirin (RBV) for 12 weeks in treatment-naïve participants with HIV-1 and genotype 2 HCV coinfection	
Reporting group title	Genotype 1 Treatment-naïve
Reporting group description: SOF + RBV for 24 weeks in treatment-naïve participants with HIV-1 and genotype 1 HCV coinfection	
Reporting group title	Genotype 2 Treatment-experienced
Reporting group description: SOF + RBV for 24 weeks in treatment-experienced participants with HIV-1 and genotype 2 HCV coinfection	
Reporting group title	Genotype 3 Treatment-naïve
Reporting group description: SOF + RBV for 24 weeks in treatment-naïve participants with HIV-1 and genotype 3 HCV coinfection	
Reporting group title	Genotype 3 Treatment-experienced
Reporting group description: SOF + RBV for 24 weeks in treatment-experienced participants with HIV-1 and genotype 3 HCV coinfection	
Reporting group title	Genotype 4 Treatment-naïve
Reporting group description: SOF + RBV for 24 weeks in treatment-naïve participants with HIV-1 and genotype 4 HCV coinfection	

Reporting group values	Genotype 2 Treatment-naïve	Genotype 1 Treatment-naïve	Genotype 2 Treatment- experienced
Number of subjects	19	112	6
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	55	45	55
standard deviation	± 8.2	± 7.6	± 10.2
Gender categorical Units: Subjects			
Female	4	12	0
Male	15	100	6
Race Units: Subjects			
Black or African American	0	1	1
White	18	104	5
Asian	0	5	0
American Indian/Alaska Native/ First Nations	1	0	0
Other	0	1	0
Not Permitted	0	1	0
Ethnicity Units: Subjects			

Hispanic or Latino	3	4	0
Not Hispanic or Latino	16	106	6
Not Permitted	0	2	0
Cirrhosis Status Units: Subjects			
No	18	95	4
Yes	1	17	2
IB28b Status			
CC, CT, and TT alleles are different forms of the IL28b gene.			
Units: Subjects			
CC	12	48	3
CT	5	45	1
TT	2	18	2
Missing	0	1	0
Hepatitis C Virus (HCV) RNA Units: Subjects			
< 6 log10 IU/mL	2	33	1
≥ 6 log10 IU/mL	17	79	5

Reporting group values	Genotype 3 Treatment-naïve	Genotype 3 Treatment-experienced	Genotype 4 Treatment-naïve
Number of subjects	57	49	31
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	47	49	47
standard deviation	± 5.4	± 6.2	± 5.9
Gender categorical Units: Subjects			
Female	19	11	7
Male	38	38	24
Race Units: Subjects			
Black or African American	0	0	1
White	54	49	29
Asian	2	0	0
American Indian/Alaska Native/ First Nations	0	0	0
Other	1	0	0
Not Permitted	0	0	1
Ethnicity Units: Subjects			
Hispanic or Latino	3	5	1
Not Hispanic or Latino	54	44	29
Not Permitted	0	0	1
Cirrhosis Status Units: Subjects			
No	54	26	23
Yes	3	23	8

IB28b Status			
CC, CT, and TT alleles are different forms of the IL28b gene.			
Units: Subjects			
CC	30	25	9
CT	21	20	14
TT	6	4	8
Missing	0	0	0
Hepatitis C Virus (HCV) RNA			
Units: Subjects			
< 6 log10 IU/mL	21	12	12
≥ 6 log10 IU/mL	36	37	19

Reporting group values	Total		
Number of subjects	274		
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	53		
Male	221		
Race			
Units: Subjects			
Black or African American	3		
White	259		
Asian	7		
American Indian/Alaska Native/ First Nations	1		
Other	2		
Not Permitted	2		
Ethnicity			
Units: Subjects			
Hispanic or Latino	16		
Not Hispanic or Latino	255		
Not Permitted	3		
Cirrhosis Status			
Units: Subjects			
No	220		
Yes	54		
IB28b Status			
CC, CT, and TT alleles are different forms of the IL28b gene.			
Units: Subjects			
CC	127		
CT	106		
TT	40		
Missing	1		
Hepatitis C Virus (HCV) RNA			

Units: Subjects			
< 6 log ₁₀ IU/mL	81		
≥ 6 log ₁₀ IU/mL	193		

End points

End points reporting groups

Reporting group title	Genotype 2 Treatment-naïve
Reporting group description: Sofosbuvir (SOF) + ribavirin (RBV) for 12 weeks in treatment-naïve participants with HIV-1 and genotype 2 HCV coinfection	
Reporting group title	Genotype 1 Treatment-naïve
Reporting group description: SOF + RBV for 24 weeks in treatment-naïve participants with HIV-1 and genotype 1 HCV coinfection	
Reporting group title	Genotype 2 Treatment-experienced
Reporting group description: SOF + RBV for 24 weeks in treatment-experienced participants with HIV-1 and genotype 2 HCV coinfection	
Reporting group title	Genotype 3 Treatment-naïve
Reporting group description: SOF + RBV for 24 weeks in treatment-naïve participants with HIV-1 and genotype 3 HCV coinfection	
Reporting group title	Genotype 3 Treatment-experienced
Reporting group description: SOF + RBV for 24 weeks in treatment-experienced participants with HIV-1 and genotype 3 HCV coinfection	
Reporting group title	Genotype 4 Treatment-naïve
Reporting group description: SOF + RBV for 24 weeks in treatment-naïve participants with HIV-1 and genotype 4 HCV coinfection	
Subject analysis set title	Genotype 1a Treatment-naïve
Subject analysis set type	Sub-group analysis
Subject analysis set description: SOF 400 mg tablet once daily + RBV tablets (1000-1200 mg daily based on weight) for 24 weeks in treatment-naïve participants with HIV-1 and genotype 1a HCV coinfection (subset of All Genotype 1 Treatment-naïve reporting group)	
Subject analysis set title	Genotype 1b Treatment-naïve
Subject analysis set type	Sub-group analysis
Subject analysis set description: SOF 400 mg tablet once daily + RBV tablets (1000-1200 mg daily based on weight) for 24 weeks in treatment-naïve participants with HIV-1 and genotype 1b HCV coinfection (subset of All Genotype 1 Treatment-naïve reporting group)	
Subject analysis set title	Genotype 2 Treatment-naïve
Subject analysis set type	Safety analysis
Subject analysis set description: SOF + RBV for 12 weeks in treatment-naïve participants with HIV-1 and genotype 2 HCV coinfection	
Subject analysis set title	Genotype 2/3 Treatment-experienced
Subject analysis set type	Safety analysis
Subject analysis set description: SOF + RBV for 24 weeks in treatment-experienced participants with HIV-1 and genotype 2 or 3 HCV coinfection	
Subject analysis set title	Genotype 1/3/4 Treatment-naïve
Subject analysis set type	Safety analysis
Subject analysis set description: SOF + RBV for 24 weeks in treatment-naïve participants with HIV-1 and genotype 1, 3, or 4 HCV coinfection	

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

End point title	Percentage of Participants With Sustained Virologic Response (SVR) at 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, < 25 IU/mL) 12 weeks following the last 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 intergroup analysis or analysis against a historic rate was planned or performed.

End point values	Genotype 2 Treatment- naïve	Genotype 1 Treatment- naïve	Genotype 2 Treatment- experienced	Genotype 3 Treatment- naïve
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	112	6	57
Units: percentage of participants				
number (not applicable)	89.5	84.8	83.3	91.2

End point values	Genotype 3 Treatment- experienced	Genotype 4 Treatment- naïve	Genotype 1a Treatment- naïve	Genotype 1b Treatment- naïve
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	49	31	100	11
Units: percentage of participants				
number (not applicable)	85.7	83.9	84	90.9

Statistical analyses

No statistical analyses for this end point

Primary: Incidence of Adverse Events Leading to Permanent Discontinuation of Study Drug(s)

End point title	Incidence of Adverse Events Leading to Permanent Discontinuation of Study Drug(s) ^[2]
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End point description:

The percentage of participants permanently discontinuing any study drug due to an adverse event was summarized.

End point type	Primary
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End point timeframe:

Up to 24 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	Genotype 2 Treatment- naïve	Genotype 2/3 Treatment- experienced	Genotype 1/3/4 Treatment- naïve	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	19	55	200	
Units: percentage of participants				
number (not applicable)	0	1.8	3.5	

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Participants With Sustained Virologic Response at 4 and 24 Weeks After Discontinuation of Therapy (SVR4 and SVR24)
End point description: SVR4 and SVR24 were defined as HCV RNA < the lower limit of quantitation (LLOQ) 4 weeks and 24 weeks following the last dose of study drug, respectively.	
End point type	Secondary
End point timeframe: Posttreatment Weeks 4 and 24	

End point values	Genotype 2 Treatment- naïve	Genotype 1 Treatment- naïve	Genotype 2 Treatment- experienced	Genotype 3 Treatment- naïve
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	112	6	57
Units: percentage of participants				
number (not applicable)				
SVR4	89.5	87.5	83.3	91.2
SVR24	89.5	83	83.3	91.2

End point values	Genotype 3 Treatment- experienced	Genotype 4 Treatment- naïve	Genotype 1a Treatment- naïve	Genotype 1b Treatment- naïve
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	48	31	100	11
Units: percentage of participants				
number (not applicable)				
SVR4	87.8	90.3	87.5	90.9
SVR24	83.7	80.6	82	90.9

Statistical analyses

No statistical analyses for this end point

Secondary: HCV RNA Change From Baseline at Week 1

End point title HCV RNA Change From Baseline at Week 1

End point description:

End point type Secondary

End point timeframe:

Baseline; Week 1

End point values	Genotype 2 Treatment- naïve	Genotype 1 Treatment- naïve	Genotype 2 Treatment- experienced	Genotype 3 Treatment- naïve
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	112	6	54
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-4.72 (± 0.573)	-4.54 (± 0.776)	-4.34 (± 0.575)	-4.41 (± 0.498)

End point values	Genotype 3 Treatment- experienced	Genotype 4 Treatment- naïve	Genotype 1a Treatment- naïve	Genotype 1b Treatment- naïve
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	48	31	100	11
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-4.33 (± 0.667)	-4.21 (± 0.665)	-4.57 (± 0.777)	-4.35 (± 0.752)

Statistical analyses

No statistical analyses for this end point

Secondary: HCV RNA Change From Baseline at Week 2

End point title HCV RNA Change From Baseline at Week 2

End point description:

End point type Secondary

End point timeframe:

Baseline; Week 2

End point values	Genotype 2 Treatment- naïve	Genotype 1 Treatment- naïve	Genotype 2 Treatment- experienced	Genotype 3 Treatment- naïve
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	111	6	55
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-5.29 (± 0.681)	-4.92 (± 0.717)	-4.98 (± 0.633)	-4.86 (± 0.677)

End point values	Genotype 3 Treatment- experienced	Genotype 4 Treatment- naïve	Genotype 1a Treatment- naïve	Genotype 1b Treatment- naïve
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	47	30	99	11
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-4.89 (± 0.776)	-4.52 (± 0.843)	-4.97 (± 0.674)	-4.55 (± 0.928)

Statistical analyses

No statistical analyses for this end point

Secondary: HCV RNA Change From Baseline at Week 4

End point title	HCV RNA Change From Baseline at Week 4
End point description:	
End point type	Secondary
End point timeframe:	
Baseline; Week 4	

End point values	Genotype 2 Treatment- naïve	Genotype 1 Treatment- naïve	Genotype 2 Treatment- experienced	Genotype 3 Treatment- naïve
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	109	6	57
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-5.33 (± 0.655)	-4.95 (± 0.72)	-5.05 (± 0.618)	-4.89 (± 0.708)

End point values	Genotype 3 Treatment- experienced	Genotype 4 Treatment- naive	Genotype 1a Treatment- naive	Genotype 1b Treatment- naive
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	49	31	97	11
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-4.84 (± 0.895)	-4.57 (± 0.846)	-5.01 (± 0.674)	-4.55 (± 0.928)

Statistical analyses

No statistical analyses for this end point

Secondary: HCV RNA Change From Baseline at Week 6

End point title	HCV RNA Change From Baseline at Week 6
End point description:	
End point type	Secondary
End point timeframe:	
Baseline; Week6	

End point values	Genotype 2 Treatment- naive	Genotype 1 Treatment- naive	Genotype 2 Treatment- experienced	Genotype 3 Treatment- naive
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	109	6	57
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-5.33 (± 0.655)	-4.95 (± 0.718)	-5.05 (± 0.618)	-4.89 (± 0.71)

End point values	Genotype 3 Treatment- experienced	Genotype 4 Treatment- naive	Genotype 1a Treatment- naive	Genotype 1b Treatment- naive
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	49	31	97	11
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-4.91 (± 0.789)	-4.57 (± 0.846)	-5.01 (± 0.672)	-4.55 (± 0.928)

Statistical analyses

No statistical analyses for this end point

Secondary: HCV RNA Change From Baseline at Week 8

End point title	HCV RNA Change From Baseline at Week 8
End point description:	
End point type	Secondary
End point timeframe:	
Baseline; Week 8	

End point values	Genotype 2 Treatment- naïve	Genotype 1 Treatment- naïve	Genotype 2 Treatment- experienced	Genotype 3 Treatment- naïve
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	109	6	56
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-5.33 (± 0.655)	-4.95 (± 0.722)	-5.05 (± 6.618)	-4.88 (± 0.708)

End point values	Genotype 3 Treatment- experienced	Genotype 4 Treatment- naïve	Genotype 1a Treatment- naïve	Genotype 1b Treatment- naïve
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	49	31	97	11
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-4.86 (± 0.876)	-4.57 (± 0.846)	-5.01 (± 0.676)	-4.55 (± 0.928)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing Virologic Failure

End point title	Percentage of Participants Experiencing Virologic Failure
End point description:	
On-treatment virologic failure was defined as either: - Virologic breakthrough (confirmed HCV RNA \geq 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 - Nonresponse (HCV RNA persistently \geq LLOQ through 8 weeks of treatment).	
Virologic relapse was defined as confirmed HCV RNA \geq LLOQ during the posttreatment period, having achieved HCV RNA $<$ LLOQ at last on-treatment visit.	
End point type	Secondary
End point timeframe:	
Baseline up to Posttreatment Week 24	

End point values	Genotype 2 Treatment- naïve	Genotype 1 Treatment- naïve	Genotype 2 Treatment- experienced	Genotype 3 Treatment- naïve
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	112	6	57
Units: percentage of participants				
number (not applicable)				
On-Treatment Virologic Failure	0	0	0	0
Virologic Relapse	5.3	12.5	16.7	7

End point values	Genotype 3 Treatment- experienced	Genotype 4 Treatment- naïve	Genotype 1a Treatment- naïve	Genotype 1b Treatment- naïve
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	49	31	100	11
Units: percentage of participants				
number (not applicable)				
On-Treatment Virologic Failure	2	0	0	0
Virologic Relapse	12.5	16.1	13	9.1

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 24 weeks plus 30 days

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.0
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Reporting groups

Reporting group title	Genotype 2 Treatment-naive
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Reporting group description:

SOF + RBV for 12 weeks in treatment-naive participants with HIV-1 and genotype 2 HCV coinfection

Reporting group title	Genotype 2/3 Treatment-experienced
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Reporting group description:

SOF + RBV for 24 weeks in treatment-experienced participants with HIV-1 and genotype 2 or 3 HCV coinfection

Reporting group title	Genotype 1/3/4 Treatment-naive
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Reporting group description:

SOF + RBV for 24 weeks in treatment-naive participants with HIV-1 and genotype 1, 3, or 4 HCV coinfection

Serious adverse events	Genotype 2 Treatment-naive	Genotype 2/3 Treatment- experienced	Genotype 1/3/4 Treatment-naive
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 19 (0.00%)	5 / 55 (9.09%)	10 / 200 (5.00%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatic cancer			
subjects affected / exposed	0 / 19 (0.00%)	1 / 55 (1.82%)	0 / 200 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 55 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			

subjects affected / exposed	0 / 19 (0.00%)	1 / 55 (1.82%)	0 / 200 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 55 (1.82%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 55 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 55 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 19 (0.00%)	1 / 55 (1.82%)	0 / 200 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 55 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Petechiae			
subjects affected / exposed	0 / 19 (0.00%)	0 / 55 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Alcoholism			

subjects affected / exposed	0 / 19 (0.00%)	1 / 55 (1.82%)	0 / 200 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug Abuse			
subjects affected / exposed	0 / 19 (0.00%)	0 / 55 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mania			
subjects affected / exposed	0 / 19 (0.00%)	0 / 55 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			
subjects affected / exposed	0 / 19 (0.00%)	0 / 55 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 19 (0.00%)	0 / 55 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Rhabdomyolysis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 55 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Atypical pneumonia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 55 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 55 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Tooth abscess			
subjects affected / exposed	0 / 19 (0.00%)	0 / 55 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Genotype 2 Treatment-naïve	Genotype 2/3 Treatment-experienced	Genotype 1/3/4 Treatment-naïve
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 19 (89.47%)	47 / 55 (85.45%)	181 / 200 (90.50%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Seborrhoeic keratosis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 55 (0.00%)	0 / 200 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 19 (5.26%)	11 / 55 (20.00%)	32 / 200 (16.00%)
occurrences (all)	1	11	36
Fatigue			
subjects affected / exposed	5 / 19 (26.32%)	11 / 55 (20.00%)	40 / 200 (20.00%)
occurrences (all)	5	12	45
Influenza like illness			
subjects affected / exposed	1 / 19 (5.26%)	0 / 55 (0.00%)	4 / 200 (2.00%)
occurrences (all)	1	0	4
Malaise			
subjects affected / exposed	1 / 19 (5.26%)	0 / 55 (0.00%)	2 / 200 (1.00%)
occurrences (all)	1	0	2
Pyrexia			
subjects affected / exposed	0 / 19 (0.00%)	3 / 55 (5.45%)	5 / 200 (2.50%)
occurrences (all)	0	3	5
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 19 (0.00%)	6 / 55 (10.91%)	17 / 200 (8.50%)
occurrences (all)	0	6	17

Dysphonia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 55 (0.00%)	0 / 200 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	2 / 19 (10.53%)	8 / 55 (14.55%)	10 / 200 (5.00%)
occurrences (all)	2	8	10
Dyspnoea exertional			
subjects affected / exposed	2 / 19 (10.53%)	5 / 55 (9.09%)	11 / 200 (5.50%)
occurrences (all)	2	5	11
Oropharyngeal discomfort			
subjects affected / exposed	1 / 19 (5.26%)	0 / 55 (0.00%)	1 / 200 (0.50%)
occurrences (all)	1	0	1
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	1 / 19 (5.26%)	0 / 55 (0.00%)	1 / 200 (0.50%)
occurrences (all)	1	0	1
Anxiety			
subjects affected / exposed	0 / 19 (0.00%)	3 / 55 (5.45%)	15 / 200 (7.50%)
occurrences (all)	0	3	15
Claustrophobia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 55 (0.00%)	0 / 200 (0.00%)
occurrences (all)	1	0	0
Depressed mood			
subjects affected / exposed	2 / 19 (10.53%)	0 / 55 (0.00%)	4 / 200 (2.00%)
occurrences (all)	2	0	4
Depression			
subjects affected / exposed	0 / 19 (0.00%)	5 / 55 (9.09%)	9 / 200 (4.50%)
occurrences (all)	0	5	10
Insomnia			
subjects affected / exposed	3 / 19 (15.79%)	5 / 55 (9.09%)	36 / 200 (18.00%)
occurrences (all)	3	5	37
Irritability			
subjects affected / exposed	1 / 19 (5.26%)	6 / 55 (10.91%)	20 / 200 (10.00%)
occurrences (all)	1	6	20
Mood swings			

subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	1 / 55 (1.82%) 1	2 / 200 (1.00%) 2
Sleep disorder subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	1 / 55 (1.82%) 1	13 / 200 (6.50%) 13
Investigations Haemoglobin decreased subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 55 (0.00%) 0	3 / 200 (1.50%) 5
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	2 / 55 (3.64%) 3	1 / 200 (0.50%) 1
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	5 / 55 (9.09%) 5	9 / 200 (4.50%) 10
Headache subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	7 / 55 (12.73%) 8	35 / 200 (17.50%) 39
Lethargy subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	1 / 55 (1.82%) 1	15 / 200 (7.50%) 15
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	3 / 55 (5.45%) 3	16 / 200 (8.00%) 16
Ear and labyrinth disorders Ear discomfort subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 55 (0.00%) 0	0 / 200 (0.00%) 0
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	3 / 55 (5.45%) 3	9 / 200 (4.50%) 9
Abdominal pain upper			

subjects affected / exposed	3 / 19 (15.79%)	1 / 55 (1.82%)	9 / 200 (4.50%)
occurrences (all)	3	1	10
Abdominal tenderness			
subjects affected / exposed	1 / 19 (5.26%)	0 / 55 (0.00%)	1 / 200 (0.50%)
occurrences (all)	1	0	1
Constipation			
subjects affected / exposed	0 / 19 (0.00%)	0 / 55 (0.00%)	10 / 200 (5.00%)
occurrences (all)	0	0	10
Diarrhoea			
subjects affected / exposed	1 / 19 (5.26%)	5 / 55 (9.09%)	24 / 200 (12.00%)
occurrences (all)	1	7	27
Gastrointestinal pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 55 (0.00%)	1 / 200 (0.50%)
occurrences (all)	1	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 19 (0.00%)	0 / 55 (0.00%)	10 / 200 (5.00%)
occurrences (all)	0	0	11
Nausea			
subjects affected / exposed	3 / 19 (15.79%)	4 / 55 (7.27%)	32 / 200 (16.00%)
occurrences (all)	3	4	33
Tongue ulceration			
subjects affected / exposed	1 / 19 (5.26%)	0 / 55 (0.00%)	0 / 200 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	0 / 19 (0.00%)	1 / 55 (1.82%)	13 / 200 (6.50%)
occurrences (all)	0	2	14
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 55 (0.00%)	2 / 200 (1.00%)
occurrences (all)	1	0	2
Jaundice			
subjects affected / exposed	1 / 19 (5.26%)	1 / 55 (1.82%)	5 / 200 (2.50%)
occurrences (all)	1	1	5
Skin and subcutaneous tissue disorders			
Alopecia			

subjects affected / exposed	0 / 19 (0.00%)	3 / 55 (5.45%)	5 / 200 (2.50%)
occurrences (all)	0	3	5
Dermatitis			
subjects affected / exposed	2 / 19 (10.53%)	1 / 55 (1.82%)	4 / 200 (2.00%)
occurrences (all)	2	1	4
Dry skin			
subjects affected / exposed	1 / 19 (5.26%)	2 / 55 (3.64%)	9 / 200 (4.50%)
occurrences (all)	1	2	10
Hair texture abnormal			
subjects affected / exposed	1 / 19 (5.26%)	0 / 55 (0.00%)	0 / 200 (0.00%)
occurrences (all)	1	0	0
Hyperhidrosis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 55 (0.00%)	2 / 200 (1.00%)
occurrences (all)	1	0	2
Pruritus			
subjects affected / exposed	0 / 19 (0.00%)	5 / 55 (9.09%)	16 / 200 (8.00%)
occurrences (all)	0	6	16
Rash			
subjects affected / exposed	2 / 19 (10.53%)	3 / 55 (5.45%)	15 / 200 (7.50%)
occurrences (all)	4	3	17
Urticaria			
subjects affected / exposed	1 / 19 (5.26%)	0 / 55 (0.00%)	1 / 200 (0.50%)
occurrences (all)	1	0	1
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	0 / 19 (0.00%)	3 / 55 (5.45%)	1 / 200 (0.50%)
occurrences (all)	0	3	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 19 (5.26%)	2 / 55 (3.64%)	11 / 200 (5.50%)
occurrences (all)	1	2	11
Back pain			
subjects affected / exposed	1 / 19 (5.26%)	2 / 55 (3.64%)	13 / 200 (6.50%)
occurrences (all)	1	2	13
Intervertebral disc protrusion			

subjects affected / exposed	1 / 19 (5.26%)	0 / 55 (0.00%)	2 / 200 (1.00%)
occurrences (all)	1	0	2
Musculoskeletal chest pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 55 (0.00%)	2 / 200 (1.00%)
occurrences (all)	1	0	2
Myalgia			
subjects affected / exposed	1 / 19 (5.26%)	6 / 55 (10.91%)	11 / 200 (5.50%)
occurrences (all)	1	7	11
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 55 (0.00%)	7 / 200 (3.50%)
occurrences (all)	1	0	7
Ear infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 55 (0.00%)	1 / 200 (0.50%)
occurrences (all)	1	0	1
Influenza			
subjects affected / exposed	0 / 19 (0.00%)	3 / 55 (5.45%)	4 / 200 (2.00%)
occurrences (all)	0	3	4
Localised infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 55 (0.00%)	1 / 200 (0.50%)
occurrences (all)	1	0	1
Nasopharyngitis			
subjects affected / exposed	3 / 19 (15.79%)	5 / 55 (9.09%)	11 / 200 (5.50%)
occurrences (all)	3	6	13
Otitis media			
subjects affected / exposed	1 / 19 (5.26%)	0 / 55 (0.00%)	1 / 200 (0.50%)
occurrences (all)	1	0	1
Pharyngitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 55 (0.00%)	3 / 200 (1.50%)
occurrences (all)	1	0	3
Rhinitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 55 (0.00%)	8 / 200 (4.00%)
occurrences (all)	1	0	9
Sinusitis			
subjects affected / exposed	1 / 19 (5.26%)	1 / 55 (1.82%)	7 / 200 (3.50%)
occurrences (all)	1	1	7

Subcutaneous abscess subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 55 (0.00%) 0	0 / 200 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	2 / 55 (3.64%) 2	13 / 200 (6.50%) 15
Urethritis gonococcal subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 55 (0.00%) 0	0 / 200 (0.00%) 0
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	2 / 55 (3.64%) 2	17 / 200 (8.50%) 17
Hyperphagia subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	3 / 55 (5.45%) 3	1 / 200 (0.50%) 1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 January 2013	<ul style="list-style-type: none">• The assessment of adverse events (AEs) text was modified to clarify the assessment of causality for AEs.
27 February 2013	<ul style="list-style-type: none">• The study design was updated to extend the treatment period for treatment-naive subjects with genotype 3 HCV infection from 12 weeks to 24 weeks.• The study design was revised to increase the number of treatment-naive subjects with genotype 2 and 3 HCV infection from 50 to 100.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/25659285>