Clinical trial results:
A Phase 2, Open-Label, Multicenter, Multi-cohort, Single-Arm Study to Investigate the Safety and Efficacy of Sofosbuvir + Ribavirin in Adolescents and Children with Genotype 2 or 3 Chronic HCV Infection

Summary

EudraCT number	2014-002283-32
Trial protocol	DE IT GB Outside EU/EEA BE
Global end of trial date	13 September 2018

Results information

Result version number	v1 (current)
This version publication date	16 March 2019
First version publication date	16 March 2019

Trial information

Trial identification

Sponsor protocol code	GS-US-334-1112

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02175758
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)	Yes
EMA paediatric investigation plan number(s)	EMEA-001276-PIP01-12
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 September 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 June 2018
Global end of trial reached?	Yes
Global end of trial date	13 September 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study will have two parts as follows:
The PK Lead-in Phase of the study will evaluate the steady state pharmacokinetics (PK) and confirm the dose of sofosbuvir (SOF) in hepatitis C virus (HCV)-infected pediatric participants. The PK Lead-in Phase will also evaluate the safety and
tolerability of 7 days of dosing of SOF+ribavirin (RBV) in HCV-infected pediatric participants.

The Treatment Phase will be initiated by age cohort after confirmation of age-appropriate SOF dosage levels. Participants from the PK Lead-in Phase will immediately rollover into the Treatment Phase with no interruption of study drug administration. The Treatment Phase will evaluate the antiviral efficacy, safety, and tolerability of SOF+RBV for 12 or 24 weeks in pediatric participants with genotype 2 or 3 HCV infection, respectively.

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	07 July 2014
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	United Kingdom: 12
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Italy: 11
Country: Number of subjects enrolled	United States: 46
Country: Number of subjects enrolled	New Zealand: 2
Country: Number of subjects enrolled	Russian Federation: 17
Country: Number of subjects enrolled	Australia: 9

Worldwide total number of subjects	106
EEA total number of subjects	32

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)	54
Adolescents (12-17 years)	52
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Australia, Europe, Russia, New Zealand, and the United States. The first participant was screened on 07 July 2014. The last study visit occurred on 13 September 2018.

Pre-assignment

Screening details:

135 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	12 to < 18 Years Old - SOF+RBV 12 Weeks

Arm description:

Participants 12 to < 18 years of age with HCV genotype 2 received SOF 400 mg (1 x 400 mg tablet, 4 x 100 mg tablets, or 8 x 50 mg oral granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Sofosbuvir
Investigational medicinal product code	
Other name	SOF, GS-7977, Sovaldi®
Pharmaceutical forms	Tablet, Granules
Routes of administration	Oral use

Dosage and administration details:

400 mg (1 x 400 mg tablet, 4 x 100 mg tablets, or 8 x 50 mg oral granules) once daily

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	RBV, REBETOL®
Pharmaceutical forms	Oral solution, Capsule
Routes of administration	Oral use

Dosage and administration details:

Up to 1400 mg, oral solution or capsules administered orally in a divided daily dose based on weight

Arm title	12 to < 18 Years Old - SOF+RBV 24 Weeks

Arm description:

Participants 12 to < 18 years of age with HCV genotype 3 received SOF 400 mg (1 x 400 mg tablet, 4 x 100 mg tablets, or 8 x 50 mg oral granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Sofosbuvir
Investigational medicinal product code	
Other name	SOF, GS-7977, Sovaldi®
Pharmaceutical forms	Granules, Tablet
Routes of administration	Oral use

Dosage and administration details:

400 mg (1 x 400 mg tablet, 4 x 100 mg tablets, or 8 x 50 mg oral granules) once daily

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	RBV, REBETOL®
Pharmaceutical forms	Capsule, Oral solution
Routes of administration	Oral use

Dosage and administration details:

Up to 1400 mg, oral solution or capsules administered orally in a divided daily dose based on weight

Arm title	6 to < 12 Years Old - SOF+RBV 12 Weeks

Arm description:

Participants 6 to < 12 years of age with HCV genotype 2 received SOF 200 mg (2 x 100 mg tablets or 4 x 50 mg oral granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Sofosbuvir
Investigational medicinal product code	
Other name	SOF, GS-7977, Sovaldi®
Pharmaceutical forms	Granules, Tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg (2 x 100 mg tablets or 4 x 50 mg oral granules) once daily

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	RBV, REBETOL®
Pharmaceutical forms	Capsule, Oral solution
Routes of administration	Oral use

Dosage and administration details:

Up to 1400 mg, oral solution or capsules administered orally in a divided daily dose based on weight

Arm title	6 to < 12 Years Old - SOF+RBV 24 Weeks

Arm description:

Participants 6 to < 12 years of age with HCV genotype 3 received SOF 200 mg (2 x 100 mg tablets or 4 x 50 mg oral granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Sofosbuvir
Investigational medicinal product code	
Other name	SOF, GS-7977, Sovaldi®
Pharmaceutical forms	Granules, Tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg (2 x 100 mg tablets or 4 x 50 mg oral granules) once daily

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	RBV, REBETOL®
Pharmaceutical forms	Capsule, Oral solution
Routes of administration	Oral use

Dosage and administration details:

Up to 1400 mg, oral solution or capsules administered orally in a divided daily dose based on weight

Arm title	3 to < 6 Years Old - SOF+RBV 12 Weeks

Arm description:

Participants 3 to < 6 years of age with HCV genotype 2 received SOF (weight ≥ 17 kg: 200 mg granules; weight < 17 kg: 150 mg granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Sofosbuvir
Investigational medicinal product code	
Other name	SOF, GS-7977, Sovaldi®
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

Weight ≥ 17 kg: 200 mg granules; weight < 17 kg: 150 mg granules once daily

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	RBV, REBETOL®
Pharmaceutical forms	Capsule, Oral solution
Routes of administration	Oral use

Dosage and administration details:

Up to 1400 mg, oral solution or capsules administered orally in a divided daily dose based on weight

Arm title	3 to < 6 Years Old - SOF+RBV 24 Weeks

Arm description:

Participants 3 to < 6 years of age with HCV genotype 3 received SOF (weight ≥ 17 kg: 200 mg granules; weight < 17 kg: 150 mg granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Sofosbuvir
Investigational medicinal product code	
Other name	SOF, GS-7977, Sovaldi®
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

Weight ≥ 17 kg: 200 mg granules; weight < 17 kg: 150 mg granules once daily

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	RBV, REBETOL®
Pharmaceutical forms	Capsule, Oral solution
Routes of administration	Oral use

Dosage and administration details:

Up to 1400 mg, oral solution or capsules administered orally in a divided daily dose based on weight

Number of subjects in period 1	12 to < 18 Years Old - SOF+RBV 12 Weeks	12 to < 18 Years Old - SOF+RBV 24 Weeks	6 to < 12 Years Old - SOF+RBV 12 Weeks
Started	13	39	13
Completed	13	38	13
Not completed	0	1	0
Adverse event, non-fatal	-	-	-
Lost to follow-up	-	1	-

Number of subjects in period 1	6 to < 12 Years Old - SOF+RBV 24 Weeks	3 to < 6 Years Old - SOF+RBV 12 Weeks	3 to < 6 Years Old - SOF+RBV 24 Weeks
Started	28	5	8

Completed	28	4	8
Not completed	0	1	0
Adverse event, non-fatal	-	1	-
Lost to follow-up	-	-	-

Baseline characteristics

Reporting groups	
Reporting group title	12 to < 18 Years Old - SOF+RBV 12 Weeks
Reporting group description:	
Participants 12 to < 18 years of age with HCV genotype 2 received SOF 400 mg (1 x 400 mg tablet, 4 x 100 mg tablets, or 8 x 50 mg oral granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 12 weeks.	
Reporting group title	12 to < 18 Years Old - SOF+RBV 24 Weeks
Reporting group description:	
Participants 12 to < 18 years of age with HCV genotype 3 received SOF 400 mg (1 x 400 mg tablet, 4 x 100 mg tablets, or 8 x 50 mg oral granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 24 weeks.	
Reporting group title	6 to < 12 Years Old - SOF+RBV 12 Weeks
Reporting group description:	
Participants 6 to < 12 years of age with HCV genotype 2 received SOF 200 mg (2 x 100 mg tablets or 4 x 50 mg oral granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 12 weeks.	
Reporting group title	6 to < 12 Years Old - SOF+RBV 24 Weeks
Reporting group description:	
Participants 6 to < 12 years of age with HCV genotype 3 received SOF 200 mg (2 x 100 mg tablets or 4 x 50 mg oral granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 24 weeks.	
Reporting group title	3 to < 6 Years Old - SOF+RBV 12 Weeks
Reporting group description:	
Participants 3 to < 6 years of age with HCV genotype 2 received SOF (weight ≥ 17 kg: 200 mg granules; weight < 17 kg: 150 mg granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 12 weeks.	
Reporting group title	3 to < 6 Years Old - SOF+RBV 24 Weeks
Reporting group description:	
Participants 3 to < 6 years of age with HCV genotype 3 received SOF (weight ≥ 17 kg: 200 mg granules; weight < 17 kg: 150 mg granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 24 weeks.	

Reporting group values	12 to < 18 Years Old - SOF+RBV 12 Weeks	12 to < 18 Years Old - SOF+RBV 24 Weeks	6 to < 12 Years Old - SOF+RBV 12 Weeks
Number of subjects	13	39	13
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	15	15	8
standard deviation	± 1.9	± 1.9	± 2.1
Gender categorical Units: Subjects			
Female	5	16	10
Male	8	23	3
Race Units: Subjects			
White	11	36	9
Asian	0	1	2

Other	0	1	2
Black or African American	2	0	0
Native Hawaiian or Pacific Islander	0	1	0
Ethnicity Units: Subjects			
Hispanic or Latino	0	2	2
Not Hispanic or Latino	13	36	11
Not Disclosed	0	1	0
HCV RNA Category Units: Subjects			
< 800,000 IU/mL	5	13	7
≥ 800,000 IU/mL	8	26	6

Reporting group values	6 to < 12 Years Old - SOF+RBV 24 Weeks	3 to < 6 Years Old - SOF+RBV 12 Weeks	3 to < 6 Years Old - SOF+RBV 24 Weeks
Number of subjects	28	5	8
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	9	4	5
standard deviation	± 1.7	± 0.8	± 0.8
Gender categorical Units: Subjects			
Female	20	4	6
Male	8	1	2
Race Units: Subjects			
White	20	3	6
Asian	6	0	1
Other	2	1	1
Black or African American	0	1	0
Native Hawaiian or Pacific Islander	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	4	1	0
Not Hispanic or Latino	23	4	8
Not Disclosed	1	0	0
HCV RNA Category Units: Subjects			
< 800,000 IU/mL	15	2	8
≥ 800,000 IU/mL	13	3	0

Reporting group values	Total		
Number of subjects	106		
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	 -		
Gender categorical Units: Subjects			
Female	61		
Male	45		
Race Units: Subjects			
White	85		
Asian	10		
Other	7		
Black or African American	3		
Native Hawaiian or Pacific Islander	1		
Ethnicity Units: Subjects			
Hispanic or Latino	9		
Not Hispanic or Latino	95		
Not Disclosed	2		
HCV RNA Category Units: Subjects			
< 800,000 IU/mL	50		
≥ 800,000 IU/mL	56		

End points reporting groups

Reporting group title	12 to < 18 Years Old - SOF+RBV 12 Weeks
Reporting group description:	
Participants 12 to < 18 years of age with HCV genotype 2 received SOF 400 mg (1 x 400 mg tablet, 4 x 100 mg tablets, or 8 x 50 mg oral granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 12 weeks.	
Reporting group title	12 to < 18 Years Old - SOF+RBV 24 Weeks
Reporting group description:	
Participants 12 to < 18 years of age with HCV genotype 3 received SOF 400 mg (1 x 400 mg tablet, 4 x 100 mg tablets, or 8 x 50 mg oral granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 24 weeks.	
Reporting group title	6 to < 12 Years Old - SOF+RBV 12 Weeks
Reporting group description:	
Participants 6 to < 12 years of age with HCV genotype 2 received SOF 200 mg (2 x 100 mg tablets or 4 x 50 mg oral granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 12 weeks.	
Reporting group title	6 to < 12 Years Old - SOF+RBV 24 Weeks
Reporting group description:	
Participants 6 to < 12 years of age with HCV genotype 3 received SOF 200 mg (2 x 100 mg tablets or 4 x 50 mg oral granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 24 weeks.	
Reporting group title	3 to < 6 Years Old - SOF+RBV 12 Weeks
Reporting group description:	
Participants 3 to < 6 years of age with HCV genotype 2 received SOF (weight ≥ 17 kg: 200 mg granules; weight < 17 kg: 150 mg granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 12 weeks.	
Reporting group title	3 to < 6 Years Old - SOF+RBV 24 Weeks
Reporting group description:	
Participants 3 to < 6 years of age with HCV genotype 3 received SOF (weight ≥ 17 kg: 200 mg granules; weight < 17 kg: 150 mg granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 24 weeks.	
Subject analysis set title	PK Lead-in: 12 to < 18 Years Old - SOF +RBV 12 or 24 Weeks
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants 12 to < 18 years of age received SOF 400 mg (1 x 400 mg tablet, 4 x 100 mg tablets, or 8 x 50 mg oral granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 12 or 24 weeks.	
Subject analysis set title	PK Lead-in: 6 to < 12 Years Old - SOF+RBV 12 or 24 Weeks
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants 6 to < 12 years of age received SOF 200 mg (2 x 100 mg tablets or 4 x 50 mg oral granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 12 or 24 weeks.	
Subject analysis set title	PK Lead-in: 3 to < 6 Years Old - SOF+RBV 12 or 24 Weeks
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants 3 to < 6 years of age received SOF (weight ≥ 17 kg: 200 mg granules; weight < 17 kg: 150 mg granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 12 or 24 weeks.	
Subject analysis set title	12 to < 18 Years Old (Total) - SOF+RBV 12 or 24 Weeks
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants 12 to < 18 years of age received SOF 400 mg (1 x 400 mg tablet, 4 x 100 mg tablets, or 8 x 50 mg oral granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on	

weight) for 12 or 24 weeks.

Subject analysis set title	3 to < 12 Years Old (Total) - SOF+RBV 12 or 24 Weeks
Subject analysis set type	Full analysis

Subject analysis set description:

Participants 6 to < 12 years of age received SOF 200 mg (2 x 100 mg tablets or 4 x 50 mg oral granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 12 or 24 weeks.
Participants 3 to < 6 years of age received SOF (weight ≥ 17 kg: 200 mg granules; weight < 17 kg: 150 mg granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 12 or 24 weeks.

Subject analysis set title	Males 12 to < 18 Years Old - SOF+RBV 12 or 24 Weeks
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Male participants 12 to < 18 years of age received SOF 400 mg (1 x 400 mg tablet, 4 x 100 mg tablets, or 8 x 50 mg oral granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 12 or 24 weeks.

Subject analysis set title	Males 6 to < 12 Years Old - SOF+RBV 12 or 24 Weeks
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Male participants 6 to < 12 years of age received SOF 200 mg (2 x 100 mg tablets or 4 x 50 mg oral granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 12 or 24 weeks.

Subject analysis set title	Males 3 to < 6 Years Old - SOF+RBV 12 or 24 Weeks
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Male participants 3 to < 6 years of age received SOF (weight ≥ 17 kg: 200 mg granules; weight < 17 kg: 150 mg granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 12 or 24 weeks.

Subject analysis set title	Females 12 to < 18 Years Old - SOF+RBV 12 or 24 Weeks
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Female participants 12 to < 18 years of age received SOF 400 mg (1 x 400 mg tablet, 4 x 100 mg tablets, or 8 x 50 mg oral granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 12 or 24 weeks.

Subject analysis set title	Females 6 to < 12 Years Old - SOF+RBV 12 or 24 Weeks
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Female participants 6 to < 12 years of age received SOF 200 mg (2 x 100 mg tablets or 4 x 50 mg oral granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 12 or 24 weeks.

Subject analysis set title	Females 3 to < 6 Years Old - SOF+RBV 12 or 24 Weeks
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Female participants 3 to < 6 years of age received SOF (weight ≥ 17 kg: 200 mg granules; weight < 17 kg: 150 mg granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 12 or 24 weeks.

Subject analysis set title	12 to < 18 Years Old - SOF+RBV 12 or 24 Weeks
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants 12 to < 18 years of age received SOF 400 mg (1 x 400 mg tablet, 4 x 100 mg tablets, or 8 x 50 mg oral granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 12 or 24 weeks.

Subject analysis set title	6 to < 12 Years Old - SOF+RBV 12 or 24 Weeks
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants 6 to < 12 years of age received SOF 200 mg (2 x 100 mg tablets or 4 x 50 mg oral granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 12 or 24 weeks.

Subject analysis set title	3 to < 6 Years Old - SOF+RBV 12 or 24 Weeks
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants 3 to < 6 years of age received SOF (weight ≥ 17 kg: 200 mg granules; weight < 17 kg: 150 mg granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 12 or 24 weeks.

Primary: For Participants in the PK Lead-in Phase, PK Parameter: AUCtau of GS-331007

End point title	For Participants in the PK Lead-in Phase, PK Parameter: AUCtau of GS-331007[1]

End point description:

AUCtau is defined as concentration of drug over time (the area under the concentration verses time curve over the dosing interval). Intensive PK Analysis Set included all participants in the PK lead-in phase who received at least 1 dose of study drug and for whom at least 1 nonmissing PK concentration value, during the intensive sampling period, was reported by the PK laboratory.

End point type	Primary

End point timeframe:

6 to < 18 years of age: predose, 0.5, 1, 2, 3, 4, 8, and 12 hours postdose on Day 7; 3 to < 6 years of age: predose, 2, 4, 8, and 12 hours postdose on Day 7

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: The statistical analysis of this primary endpoint is provided in the attachment. AUCtau of GS-331007 was compared against historical data collected in adult Phase 2/3 studies. Equivalence was determined if the 90% confidence intervals (CI) were within the predefined equivalence boundaries of 50% to 200% for all age groups.

End point values	PK Lead-in: 12 to < 18 Years Old - SOF +RBV 12 or 24 Weeks	PK Lead-in: 6 to < 12 Years Old - SOF+RBV 12 or 24 Weeks	PK Lead-in: 3 to < 6 Years Old - SOF+RBV 12 or 24 Weeks	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	10	10	
Units: h*ng/mL				
arithmetic mean (standard deviation)	9106.0 (± 2601.96)	7651.2 (± 1723.32)	10293.7 (± 1860.57)	

Attachments (see zip file)	Statistical Analysis/334-1112_Primary_Endpoint_StatsAnalysis.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Permanently Discontinued Any Study Drug Due to an Adverse Event During the PK Lead-in Phase or the Treatment Phase

End point title	Percentage of Participants Who Permanently Discontinued Any Study Drug Due to an Adverse Event During the PK Lead-in Phase or the Treatment Phase[2]

End point description:

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

End point type	Primary

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 comparison was planned or performed.

End point values	12 to < 18 Years Old - SOF+RBV 12 Weeks	12 to < 18 Years Old - SOF+RBV 24 Weeks	6 to < 12 Years Old - SOF+RBV 12 Weeks	6 to < 12 Years Old - SOF+RBV 24 Weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	39	13	28
Units: percentage of participants				
number (not applicable)	0	0	0	0

End point values	3 to < 6 Years Old - SOF+RBV 12 Weeks	3 to < 6 Years Old - SOF+RBV 24 Weeks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	8		
Units: percentage of participants				
number (not applicable)	20.0	0		

Statistical analyses

No statistical analyses for this end point

Primary: For the Treatment Phase, Percentage of Participants With SVR at 12 Weeks After Discontinuation of Therapy (SVR12)

End point title	For the Treatment Phase, Percentage of Participants With SVR at 12 Weeks After Discontinuation of Therapy (SVR12)[3]

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.

End point type	Primary

End point timeframe:

Posttreatment Week 12

Notes:

[3] - 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: The statistical analysis of this primary endpoint is provided in the attachment. The SVR12 rate for the 12 to < 18 Years Old group was compared with the historical SVR12 rate of 80% using a 2-sided exact 1-sample binomial test at the 0.05 significance level. If superiority was demonstrated in the 12 to < 18 Years Old group, then the SVR12 rate for participants aged 3 to < 12 years would be compared with 80% at the 0.05 significance level.

End point values	12 to < 18 Years Old - SOF+RBV 12 Weeks	12 to < 18 Years Old - SOF+RBV 24 Weeks	6 to < 12 Years Old - SOF+RBV 12 Weeks	6 to < 12 Years Old - SOF+RBV 24 Weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	39	13	28
Units: percentage of participants				
number (confidence interval 95%)	100.0 (75.3 to 100.0)	97.4 (86.5 to 99.9)	100.0 (75.3 to 100.0)	100.0 (87.7 to 100.0)

End point values	3 to < 6 Years Old - SOF+RBV 12 Weeks	3 to < 6 Years Old - SOF+RBV 24 Weeks	12 to < 18 Years Old (Total) - SOF+RBV 12 or 24 Weeks	3 to < 12 Years Old (Total) - SOF+RBV 12 or 24 Weeks
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	5	8	52	54
Units: percentage of participants				
number (confidence interval 95%)	80.0 (28.4 to 99.5)	100.0 (63.1 to 100.0)	98.1 (89.7 to 100.0)	98.1 (90.1 to 100.0)

Attachments (see zip file)	Statistical Analysis/334-

Statistical analyses

No statistical analyses for this end point

Secondary: For Participants in the PK Lead-in Phase, Change From Baseline in HCV RNA

End point title	For Participants in the PK Lead-in Phase, Change From Baseline in HCV RNA

End point description:

Participants who were enrolled in the PK lead-in phase with available data were analyzed. 999 = Not Applicable; Participants from the 12 Weeks groups were not analyzed for Change at Weeks 16, 20, and 24 because they were only treated for 12 weeks.

End point type	Secondary

End point timeframe:

Baseline; Weeks 1, 2, 4, 8, and 12, 16 (24 Week groups only), 20 (24 Week groups only), and 24 (24 Week groups only)

End point values	12 to < 18 Years Old - SOF+RBV 12 Weeks	12 to < 18 Years Old - SOF+RBV 24 Weeks	6 to < 12 Years Old - SOF+RBV 12 Weeks	6 to < 12 Years Old - SOF+RBV 24 Weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	2	10
Units: log10 IU/mL				
arithmetic mean (standard deviation)				

Change at Week 1 (N = 4, 6, 2, 10, 4, 8)	-3.98 (± 1.056)	-4.23 (± 0.765)	-3.82 (± 0.447)	-3.78 (± 1.234)
Change at Week 2 (N = 4, 6, 2, 9, 4, 8)	-4.84 (± 0.743)	-4.34 (± 0.758)	-4.92 (± 0.674)	-4.56 (± 1.553)
Change at Week 4 (N = 4, 6, 2, 10, 4, 8)	-4.84 (± 0.743)	-4.34 (± 0.758)	-4.92 (± 0.674)	-4.60 (± 1.686)
Change at Week 8 (N = 4, 6, 2, 10, 4, 8)	-4.84 (± 0.743)	-4.34 (± 0.758)	-4.92 (± 0.674)	-4.61 (± 1.700)
Change at Week 12 (N = 4, 6, 2, 10, 4, 8)	-4.84 (± 0.743)	-4.34 (± 0.758)	-4.92 (± 0.674)	-4.61 (± 1.700)
Change at Week 16 (N = NA, 6, NA, 10, NA, 8)	999 (± 999)	-4.34 (± 0.758)	999 (± 999)	-4.61 (± 1.700)
Change at Week 20 (N = NA, 6, NA, 10, NA, 8)	999 (± 999)	-4.34 (± 0.758)	999 (± 999)	-4.61 (± 1.700)
Change at Week 24 (N = NA, 6, NA, 10, NA, 8)	999 (± 999)	-4.34 (± 0.758)	999 (± 999)	-4.61 (± 1.700)

End point values	3 to < 6 Years Old - SOF+RBV 12 Weeks	3 to < 6 Years Old - SOF+RBV 24 Weeks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	8		
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Change at Week 1 (N = 4, 6, 2, 10, 4, 8)	-4.12 (± 0.632)	-3.53 (± 0.347)		
Change at Week 2 (N = 4, 6, 2, 9, 4, 8)	-4.31 (± 0.846)	-3.94 (± 0.422)		
Change at Week 4 (N = 4, 6, 2, 10, 4, 8)	-4.42 (± 1.006)	-3.97 (± 0.453)		
Change at Week 8 (N = 4, 6, 2, 10, 4, 8)	-4.52 (± 1.177)	-3.97 (± 0.453)		
Change at Week 12 (N = 4, 6, 2, 10, 4, 8)	-4.52 (± 1.177)	-3.97 (± 0.453)		
Change at Week 16 (N = NA, 6, NA, 10, NA, 8)	999 (± 999)	-3.97 (± 0.453)		
Change at Week 20 (N = NA, 6, NA, 10, NA, 8)	999 (± 999)	-3.97 (± 0.453)		
Change at Week 24 (N = NA, 6, NA, 10, NA, 8)	999 (± 999)	-3.97 (± 0.453)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Permanently Discontinued Any Study Drug Due to an Adverse Event During the PK Lead-in Phase

End point title	Percentage of Participants Who Permanently Discontinued Any Study Drug Due to an Adverse Event During the PK Lead-in Phase

End point description:

Participants who were enrolled in the PK lead-in phase were analyzed.

End point type	Secondary

End point timeframe:

Up to Day 7

End point values	PK Lead-in: 12 to < 18 Years Old - SOF +RBV 12 or 24 Weeks	PK Lead-in: 6 to < 12 Years Old - SOF+RBV 12 or 24 Weeks	PK Lead-in: 3 to < 6 Years Old - SOF+RBV 12 or 24 Weeks	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	12	12	
Units: percentage of participants				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: For the Treatment Phase, Percentage of Participants With Sustained Virologic Response (SVR) at 4 Weeks After Discontinuation of Therapy (SVR4)

End point title	For the Treatment Phase, Percentage of Participants With Sustained Virologic Response (SVR) 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	12 to < 18 Years Old - SOF+RBV 12 Weeks	12 to < 18 Years Old - SOF+RBV 24 Weeks	6 to < 12 Years Old - SOF+RBV 12 Weeks	6 to < 12 Years Old - SOF+RBV 24 Weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	39	13	28
Units: percentage of participants				
number (confidence interval 95%)	100.0 (75.3 to 100.0)	100.0 (91.0 to 100.0)	100.0 (75.3 to 100.0)	100.0 (87.7 to 100.0)

End point values	3 to < 6 Years Old - SOF+RBV 12 Weeks	3 to < 6 Years Old - SOF+RBV 24 Weeks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	8		
Units: percentage of participants				

number (confidence interval 95%)	80.0 (28.4 to 99.5)	100.0 (63.1 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: For the Treatment Phase, Percentage of Participants With SVR at 24 Weeks After Discontinuation of Therapy (SVR24)

End point title	For the Treatment Phase, Percentage of Participants With SVR 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. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Posttreatment Week 24

End point values	12 to < 18 Years Old - SOF+RBV 12 Weeks	12 to < 18 Years Old - SOF+RBV 24 Weeks	6 to < 12 Years Old - SOF+RBV 12 Weeks	6 to < 12 Years Old - SOF+RBV 24 Weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	39	13	28
Units: percentage of participants				
number (confidence interval 95%)	100.0 (75.3 to 100.0)	97.4 (86.5 to 99.9)	100.0 (75.3 to 100.0)	100.0 (87.7 to 100.0)

End point values	3 to < 6 Years Old - SOF+RBV 12 Weeks	3 to < 6 Years Old - SOF+RBV 24 Weeks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	8		
Units: percentage of participants				
number (confidence interval 95%)	80.0 (28.4 to 99.5)	100.0 (63.1 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: For the Treatment Phase, Percentage of Participants Experiencing Viral Breakthrough

End point title	For the Treatment Phase, Percentage of Participants Experiencing Viral Breakthrough

End point description:

Viral breakthrough was defined as having confirmed HCV RNA ≥ LLOQ after having previously had HCV RNA < LLOQ while on treatment. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Up to 24 weeks

End point values	12 to < 18 Years Old - SOF+RBV 12 Weeks	12 to < 18 Years Old - SOF+RBV 24 Weeks	6 to < 12 Years Old - SOF+RBV 12 Weeks	6 to < 12 Years Old - SOF+RBV 24 Weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	39	13	28
Units: percentage of participants				
number (not applicable)	0	0	0	0

End point values	3 to < 6 Years Old - SOF+RBV 12 Weeks	3 to < 6 Years Old - SOF+RBV 24 Weeks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	8		
Units: percentage of participants				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: For the Treatment Phase, Percentage of Participants Experiencing Viral Relapse

End point title	For the Treatment Phase, Percentage of Participants Experiencing Viral Relapse

End point description:

Viral relapse was defined as having confirmed HCV RNA ≥ 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 24

End point values	12 to < 18 Years Old - SOF+RBV 12 Weeks	12 to < 18 Years Old - SOF+RBV 24 Weeks	6 to < 12 Years Old - SOF+RBV 12 Weeks	6 to < 12 Years Old - SOF+RBV 24 Weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	39	13	28
Units: percentage of participants				
number (not applicable)	0	0	0	0

End point values	3 to < 6 Years Old - SOF+RBV 12 Weeks	3 to < 6 Years Old - SOF+RBV 24 Weeks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	8		
Units: percentage of participants				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: For the Treatment Phase, Change From Baseline in HCV RNA

End point title	For the Treatment Phase, Change From Baseline in HCV RNA

End point description:

Participants in the Full Analysis Set with available data were analyzed. 999 = Not Applicable; Participants from the 12 Weeks groups were not analyzed for Change at Weeks 16, 20, and 24 because they were only treated for 12 weeks.

End point type	Secondary

End point timeframe:

Baseline; Weeks 1, 2, 4, 8, 12, 16 (24 Week groups only), 20 (24 Week groups only), and 24 (24 Week groups only)

End point values	12 to < 18 Years Old - SOF+RBV 12 Weeks	12 to < 18 Years Old - SOF+RBV 24 Weeks	6 to < 12 Years Old - SOF+RBV 12 Weeks	6 to < 12 Years Old - SOF+RBV 24 Weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	39	13	28
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Change at Week 1 (N = 13, 38, 13, 28, 4, 8)	-4.25 (± 0.986)	-4.12 (± 0.733)	-4.12 (± 0.692)	-3.88 (± 0.928)
Change at Week 2 (N = 13, 39, 13, 27, 4, 8)	-4.74 (± 0.980)	-4.86 (± 0.702)	-4.55 (± 0.812)	-4.51 (± 1.102)
Change at Week 4 (N = 13, 39, 13, 28, 4, 8)	-4.74 (± 0.980)	-5.01 (± 0.760)	-4.68 (± 0.843)	-4.56 (± 1.171)
Change at Week 8 (N = 13, 39, 13, 28, 4, 8)	-4.74 (± 0.980)	-5.02 (± 0.771)	-4.68 (± 0.843)	-4.54 (± 1.191)

Change at Week 12 (N = 13, 39, 13, 28, 4, 8)	-4.74 (± 0.980)	-5.02 (± 0.771)	-4.68 (± 0.843)	-4.57 (± 1.178)
Change at Week 16 (N = NA, 39, NA, 28, NA, 8)	999 (± 999)	-5.02 (± 0.771)	999 (± 999)	-4.57 (± 1.178)
Change at Week 20 (N = NA, 39, NA, 28, NA, 8)	999 (± 999)	-5.02 (± 0.771)	999 (± 999)	-4.57 (± 1.178)
Change at Week 24 (N = NA, 39, NA, 28, NA, 8)	999 (± 999)	-5.02 (± 0.771)	999 (± 999)	-4.57 (± 1.178)

End point values	3 to < 6 Years Old - SOF+RBV 12 Weeks	3 to < 6 Years Old - SOF+RBV 24 Weeks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	8		
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Change at Week 1 (N = 13, 38, 13, 28, 4, 8)	-4.12 (± 0.632)	-3.53 (± 0.347)		
Change at Week 2 (N = 13, 39, 13, 27, 4, 8)	-4.31 (± 0.846)	-3.94 (± 0.422)		
Change at Week 4 (N = 13, 39, 13, 28, 4, 8)	-4.42 (± 1.006)	-3.97 (± 0.453)		
Change at Week 8 (N = 13, 39, 13, 28, 4, 8)	-4.52 (± 1.177)	-3.97 (± 0.453)		
Change at Week 12 (N = 13, 39, 13, 28, 4, 8)	-4.52 (± 1.177)	-3.97 (± 0.453)		
Change at Week 16 (N = NA, 39, NA, 28, NA, 8)	999 (± 999)	-3.97 (± 0.453)		
Change at Week 20 (N = NA, 39, NA, 28, NA, 8)	999 (± 999)	-3.97 (± 0.453)		
Change at Week 24 (N = NA, 39, NA, 28, NA, 8)	999 (± 999)	-3.97 (± 0.453)		

Statistical analyses

No statistical analyses for this end point

Secondary: For the Treatment Phase, Percentage of Participants With HCV RNA < LLOQ While On Treatment

End point title	For the Treatment Phase, Percentage of Participants With HCV RNA < LLOQ While On Treatment

End point description:

Participants in the Full Analysis Set with available data were analyzed. 999, 9999, 99999 = Not Applicable; Participants from the 12 Weeks groups were not analyzed for Weeks 16, 20, and 24 because they were only treated for 12 weeks.

End point type	Secondary

End point timeframe:

Weeks 1, 2, 4, 8, 12, 16 (24 Week groups only), 20 (24 Week groups only), and 24 (24 Week groups only)

End point values	12 to < 18 Years Old - SOF+RBV 12 Weeks	12 to < 18 Years Old - SOF+RBV 24 Weeks	6 to < 12 Years Old - SOF+RBV 12 Weeks	6 to < 12 Years Old - SOF+RBV 24 Weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	39	13	28
Units: percentage of participants				
number (confidence interval 95%)				
Week 1 (N = 13, 39, 13, 28, 4, 8)	30.8 (9.1 to 61.4)	30.8 (17.0 to 47.6)	46.2 (19.2 to 74.9)	39.3 (21.5 to 59.4)
Week 2 (N = 13, 39, 13, 28, 4, 8)	100.0 (75.3 to 100.0)	74.4 (57.9 to 87.0)	76.9 (46.2 to 95.0)	78.6 (59.0 to 91.7)
Week 4 (N = 13, 39, 13, 28, 4, 8)	100.0 (75.3 to 100.0)	92.3 (79.1 to 98.4)	100.0 (75.3 to 100.0)	96.4 (81.7 to 99.9)
Week 8 (N = 13, 39, 13, 28, 4, 8)	100.0 (75.3 to 100.0)	100.0 (91.0 to 100.0)	100.0 (75.3 to 100.0)	96.4 (81.7 to 99.9)
Week 12 (N = 13, 39, 13, 28, 4, 8)	100.0 (75.3 to 100.0)	100.0 (91.0 to 100.0)	100.0 (75.3 to 100.0)	100.0 (87.7 to 100.0)
Week 16 (N = NA, 39, NA, 28, NA, 8)	9999 (999 to 99999)	100.0 (91.0 to 100.0)	9999 (999 to 99999)	100.0 (87.7 to 100.0)
Week 20 (N = NA, 39, NA, 28, NA, 8)	9999 (999 to 99999)	100.0 (91.0 to 100.0)	9999 (999 to 99999)	100.0 (87.7 to 100.0)
Week 24 (N = NA, 39, NA, 28, NA, 8)	9999 (999 to 99999)	100.0 (91.0 to 100.0)	9999 (999 to 99999)	100.0 (87.7 to 100.0)

End point values	3 to < 6 Years Old - SOF+RBV 12 Weeks	3 to < 6 Years Old - SOF+RBV 24 Weeks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	8		
Units: percentage of participants				
number (confidence interval 95%)				
Week 1 (N = 13, 39, 13, 28, 4, 8)	50.0 (6.8 to 93.2)	37.5 (8.5 to 75.5)		
Week 2 (N = 13, 39, 13, 28, 4, 8)	75.0 (19.4 to 99.4)	87.5 (47.3 to 99.7)		
Week 4 (N = 13, 39, 13, 28, 4, 8)	75.0 (19.4 to 99.4)	100.0 (63.1 to 100.0)		
Week 8 (N = 13, 39, 13, 28, 4, 8)	100.0 (39.8 to 100.0)	100.0 (63.1 to 100.0)		
Week 12 (N = 13, 39, 13, 28, 4, 8)	100.0 (39.8 to 100.0)	100.0 (63.1 to 100.0)		
Week 16 (N = NA, 39, NA, 28, NA, 8)	9999 (999 to 99999)	100.0 (63.1 to 100.0)		
Week 20 (N = NA, 39, NA, 28, NA, 8)	9999 (999 to 99999)	100.0 (63.1 to 100.0)		
Week 24 (N = NA, 39, NA, 28, NA, 8)	9999 (999 to 99999)	100.0 (63.1 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: For the Treatment Phase, Percentage of Participants With Alanine Aminotransferase (ALT) Normalization

End point title	For the Treatment Phase, Percentage of Participants With Alanine Aminotransferase (ALT) Normalization

End point description:

ALT normalization was defined as ALT > the upper limit of normal (ULN) at baseline and ALT ≤ ULN at each visit. Participants in the Full Analysis Set with ALT > ULN at Baseline with available data were analyzed. 999 = Not Applicable; Participants from the 12 Weeks groups were not analyzed for Weeks 16, 20, and 24 because they were only treated for 12 weeks.

End point type	Secondary

End point timeframe:

Weeks 1, 2, 4, 8, 12, 16 (24 Week groups only), 20 (24 Week groups only), and 24 (24 Week groups only), and Posttreatment Week 4

End point values	12 to < 18 Years Old - SOF+RBV 12 Weeks	12 to < 18 Years Old - SOF+RBV 24 Weeks	6 to < 12 Years Old - SOF+RBV 12 Weeks	6 to < 12 Years Old - SOF+RBV 24 Weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	22	4	16
Units: percentage of participants				
number (not applicable)				
Week 1 (N = 4, 22, 4, 16, 2)	50.0	63.6	25.0	75.0
Week 2 (N = 4, 22, 3, 15, 2)	100.0	90.9	100.0	93.3
Week 4 (N = 3, 22, 4, 15, 2)	100.0	95.5	100.0	100.0
Week 8 (N = 4, 22, 3, 15, 2)	100.0	95.5	100.0	100.0
Week 12 (N = 4, 22, 4, 16, 2)	100.0	100.0	100.0	100.0
Week 16 (N = NA, 21, NA, 15, 2)	999	100.0	999	100.0
Week 20 (N = NA, 22, NA, 16, 2)	999	100.0	999	100.0
Week 24 (N = NA, 21, NA, 15, 2)	999	100.0	999	100.0
Posttreatment Week 4 (N = 4, 16, 3, 12, 2)	100.0	100.0	100.0	100.0

End point values	3 to < 6 Years Old - SOF+RBV 12 Weeks	3 to < 6 Years Old - SOF+RBV 24 Weeks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[4]	2		
Units: percentage of participants				
number (not applicable)				
Week 1 (N = 4, 22, 4, 16, 2)		100.0		
Week 2 (N = 4, 22, 3, 15, 2)		100.0		
Week 4 (N = 3, 22, 4, 15, 2)		100.0		
Week 8 (N = 4, 22, 3, 15, 2)		100.0		
Week 12 (N = 4, 22, 4, 16, 2)		100.0		
Week 16 (N = NA, 21, NA, 15, 2)		100.0		
Week 20 (N = NA, 22, NA, 16, 2)		100.0		
Week 24 (N = NA, 21, NA, 15, 2)		100.0		
Posttreatment Week 4 (N = 4, 16, 3, 12, 2)		100.0		

Notes:

[4] - 1 participant had ALT > ULN at Baseline, but no other available data.

Statistical analyses

No statistical analyses for this end point

Secondary: For the Treatment Phase, Change From Baseline in Height

End point title	For the Treatment Phase, Change From Baseline in Height

End point description:

Participants in the Safety Analysis Set with available data were analyzed. 999 = Not Applicable; Participants from the 12 Weeks groups were not analyzed for Change at Weeks 16, 20, and 24 because they were only treated for 12 weeks.

End point type	Secondary

End point timeframe:

Baseline; Weeks 1, 2, 4, 8, 12, 16 (24 Week groups only), 20 (24 Week groups only), and 24 (24 Week groups only), and Posttreatment Weeks 4, 12, and 24

End point values	12 to < 18 Years Old - SOF+RBV 12 Weeks	12 to < 18 Years Old - SOF+RBV 24 Weeks	6 to < 12 Years Old - SOF+RBV 12 Weeks	6 to < 12 Years Old - SOF+RBV 24 Weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	39	13	28
Units: centimeters				
arithmetic mean (standard deviation)				
Change at Week 1 (N = 13, 39, 13, 28, 4, 8)	0.1 (± 1.10)	0.0 (± 0.57)	0.0 (± 0.57)	0.0 (± 0.73)
Change at Week 2 (N = 13, 39, 13, 28, 4, 8)	0.1 (± 1.07)	-0.1 (± 0.59)	0.1 (± 0.66)	0.0 (± 0.54)
Change at Week 4 (N = 13, 39, 13, 28, 4, 8)	0.2 (± 1.20)	0.2 (± 0.78)	0.3 (± 0.67)	0.4 (± 0.74)
Change at Week 8 (N = 13, 39, 13, 28, 4, 8)	0.3 (± 1.27)	0.2 (± 0.85)	1.0 (± 1.00)	0.4 (± 0.62)
Change at Week 12 (N = 12, 39, 13, 28, 4, 8)	0.5 (± 1.68)	0.3 (± 0.95)	0.8 (± 0.81)	0.7 (± 0.68)
Change at Week 16 (N = NA, 38, NA, 28, NA, 8)	999 (± 999)	0.4 (± 0.91)	999 (± 999)	1.1 (± 0.93)
Change at Week 20 (N = NA, 39, NA, 28, NA, 8)	999 (± 999)	0.5 (± 1.10)	999 (± 999)	1.6 (± 1.15)
Change at Week 24 (N = NA, 36, NA, 27, NA, 8)	999 (± 999)	0.8 (± 1.54)	999 (± 999)	2.1 (± 0.88)
Change at PT Week 4 (N = 13, 38, 13, 28, 4, 8)	0.5 (± 1.79)	0.9 (± 1.70)	1.4 (± 0.80)	2.6 (± 1.17)
Change at PT Week 12 (N = 12, 38, 13, 28, 4, 8)	1.4 (± 1.65)	1.3 (± 1.90)	2.4 (± 1.02)	3.8 (± 1.30)
Change at PT Week 24 (N = 13, 37, 13, 27, 3, 8)	1.6 (± 1.89)	1.8 (± 2.83)	4.2 (± 1.11)	5.1 (± 1.59)

End point values	3 to < 6 Years Old - SOF+RBV 12 Weeks	3 to < 6 Years Old - SOF+RBV 24 Weeks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	8		
Units: centimeters				
arithmetic mean (standard deviation)				
Change at Week 1 (N = 13, 39, 13, 28, 4, 8)	0.3 (± 1.12)	0.3 (± 0.75)		
Change at Week 2 (N = 13, 39, 13, 28, 4, 8)	0.7 (± 1.09)	0.3 (± 0.50)		
Change at Week 4 (N = 13, 39, 13, 28, 4, 8)	0.9 (± 0.87)	0.5 (± 0.67)		
Change at Week 8 (N = 13, 39, 13, 28, 4, 8)	0.9 (± 0.72)	0.8 (± 0.51)		
Change at Week 12 (N = 12, 39, 13, 28, 4, 8)	1.5 (± 0.45)	1.7 (± 1.84)		
Change at Week 16 (N = NA, 38, NA, 28, NA, 8)	999 (± 999)	1.8 (± 0.79)		
Change at Week 20 (N = NA, 39, NA, 28, NA, 8)	999 (± 999)	2.5 (± 1.01)		
Change at Week 24 (N = NA, 36, NA, 27, NA, 8)	999 (± 999)	2.7 (± 1.05)		
Change at PT Week 4 (N = 13, 38, 13, 28, 4, 8)	1.6 (± 0.91)	3.5 (± 0.85)		
Change at PT Week 12 (N = 12, 38, 13, 28, 4, 8)	2.8 (± 1.81)	4.0 (± 0.95)		
Change at PT Week 24 (N = 13, 37, 13, 27, 3, 8)	5.0 (± 1.61)	5.7 (± 1.27)		

Statistical analyses

No statistical analyses for this end point

Secondary: For the Treatment Phase, Change From Baseline in Weight

End point title	For the Treatment Phase, Change From Baseline in Weight

End point description:

Participants in the Safety Analysis Set with available data were analyzed. 999 = Not Applicable; Participants from the 12 Weeks groups were not analyzed for Change at Weeks 16, 20, and 24 because they were only treated for 12 weeks.

End point type	Secondary

End point timeframe:

Baseline; Weeks 1, 2, 4, 8, 12, 16 (24 Week groups only), 20 (24 Week groups only), and 24 (24 Week groups only), and Posttreatment Weeks 4, 12, and 24

End point values	12 to < 18 Years Old - SOF+RBV 12 Weeks	12 to < 18 Years Old - SOF+RBV 24 Weeks	6 to < 12 Years Old - SOF+RBV 12 Weeks	6 to < 12 Years Old - SOF+RBV 24 Weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	39	13	28
Units: kilograms				
arithmetic mean (standard deviation)				
Change at Week 1 (N = 13, 39, 13, 28, 4, 8)	-0.7 (± 1.28)	-0.4 (± 1.36)	0.2 (± 0.82)	0.0 (± 0.55)
Change at Week 2 (N = 13, 39, 13, 28, 4, 8)	-0.2 (± 0.87)	-0.3 (± 0.99)	0.3 (± 1.08)	0.0 (± 0.64)
Change at Week 4 (N = 13, 39, 13, 28, 4, 8)	-0.2 (± 1.67)	-0.1 (± 1.15)	0.4 (± 0.90)	0.1 (± 0.90)
Change at Week 8 (N = 13, 39, 13, 28, 4, 8)	-0.5 (± 2.39)	0.0 (± 1.53)	0.6 (± 1.57)	0.1 (± 1.21)
Change at Week 12 (N = 13, 39, 13, 28, 4, 8)	-0.4 (± 2.62)	-0.1 (± 2.01)	0.9 (± 2.15)	0.5 (± 1.35)
Change at Week 16 (N = NA, 38, NA, 28, NA, 8)	999 (± 999)	0.2 (± 2.35)	999 (± 999)	0.6 (± 1.34)
Change at Week 20 (N = NA, 39, NA, 28, NA, 8)	999 (± 999)	0.1 (± 2.65)	999 (± 999)	0.9 (± 1.59)
Change at Week 24 (N = NA, 36, NA, 27, NA, 8)	999 (± 999)	0.5 (± 3.13)	999 (± 999)	1.2 (± 1.91)
Change at PT Week 4 (N = 13, 38, 13, 28, 4, 8)	-0.3 (± 3.19)	0.9 (± 3.24)	1.2 (± 2.20)	1.3 (± 2.19)
Change at PT Week 12 (N = 13, 38, 13, 28, 4, 8)	0.9 (± 2.69)	2.1 (± 3.73)	2.1 (± 3.28)	2.2 (± 2.21)
Change at PT Week 24 (N = 13, 37, 13, 27, 3, 8)	2.5 (± 4.98)	3.0 (± 4.62)	3.8 (± 3.67)	3.5 (± 2.42)

End point values	3 to < 6 Years Old - SOF+RBV 12 Weeks	3 to < 6 Years Old - SOF+RBV 24 Weeks		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	8		
Units: kilograms				
arithmetic mean (standard deviation)				
Change at Week 1 (N = 13, 39, 13, 28, 4, 8)	0.2 (± 0.10)	-0.2 (± 0.51)		
Change at Week 2 (N = 13, 39, 13, 28, 4, 8)	0.5 (± 0.21)	-0.1 (± 0.50)		
Change at Week 4 (N = 13, 39, 13, 28, 4, 8)	0.0 (± 0.22)	-0.1 (± 0.49)		
Change at Week 8 (N = 13, 39, 13, 28, 4, 8)	0.3 (± 0.14)	0.0 (± 0.55)		
Change at Week 12 (N = 13, 39, 13, 28, 4, 8)	0.3 (± 0.22)	0.1 (± 0.85)		
Change at Week 16 (N = NA, 38, NA, 28, NA, 8)	999 (± 999)	0.1 (± 0.76)		
Change at Week 20 (N = NA, 39, NA, 28, NA, 8)	999 (± 999)	0.4 (± 0.86)		
Change at Week 24 (N = NA, 36, NA, 27, NA, 8)	999 (± 999)	0.4 (± 1.03)		
Change at PT Week 4 (N = 13, 38, 13, 28, 4, 8)	0.5 (± 0.27)	0.7 (± 1.05)		

Change at PT Week 12 (N = 13, 38, 13, 28, 4, 8)	1.0 (± 0.88)	0.9 (± 1.12)		
Change at PT Week 24 (N = 13, 37, 13, 27, 3, 8)	1.3 (± 1.10)	1.7 (± 1.28)		

Statistical analyses

No statistical analyses for this end point

Secondary: For the Treatment Phase, Number of Male Participants With a Change From Baseline in Tanner Stage for Pubic Hair

End point title	For the Treatment Phase, Number of Male Participants With a Change From Baseline in Tanner Stage for Pubic Hair

End point description:

Tanner Stages is a scale that defines physical measurements of development based on external primary and secondary sex characteristics. It was used in this study to assess pubertal development with values ranging from Stage 1 (pre-pubertal characteristics) to Stage 5 (adult or mature characteristics). Any shifts (increase or decrease) in Tanner Stage from Baseline were analyzed and presented. Male participants in the Safety Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; End of Treatment (either Week 12 or 24), Posttreatment Week 12, and Posttreatment Week 24

End point values	Males 12 to < 18 Years Old - SOF+RBV 12 or 24 Weeks	Males 6 to < 12 Years Old - SOF+RBV 12 or 24 Weeks	Males 3 to < 6 Years Old - SOF+RBV 12 or 24 Weeks	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	31	11	3	
Units: participants				
End of Treatment - No Change (N = 31, 11, 3)	23	10	3	
End of Treatment - Increase (N = 31, 11, 3)	8	1	0	
End of Treatment - Decrease (N = 31, 11, 3)	0	0	0	
Posttreatment Week 12 - No Change (N = 30, 11, 3)	20	9	3	
Posttreatment Week 12 - Increase (N = 30, 11, 3)	10	2	0	
Posttreatment Week 12 - Decrease (N = 30, 11, 3)	0	0	0	
Posttreatment Week 24 - No Change (N = 31, 11, 3)	20	9	3	
Posttreatment Week 24 - Increase (N = 31, 11, 3)	11	2	0	
Posttreatment Week 24 - Decrease (N = 31, 11, 3)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: For the Treatment Phase, Number of Male Participants With a Change From Baseline in Tanner Stage for Genitalia Development

End point title	For the Treatment Phase, Number of Male Participants With a Change From Baseline in Tanner Stage for Genitalia Development

End point description:

Tanner Stages is a scale that defines physical measurements of development based on external primary and secondary sex characteristics. It was used in this study to assess pubertal development with values ranging from Stage 1 (pre-pubertal characteristics) to Stage 5 (adult or mature characteristics). Any shifts (increase or decrease) in Tanner Stage from Baseline were analyzed and presented. Male participants in the Safety Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; End of Treatment (either Week 12 or 24), Posttreatment Week 12, and Posttreatment Week 24

End point values	Males 12 to < 18 Years Old - SOF+RBV 12 or 24 Weeks	Males 6 to < 12 Years Old - SOF+RBV 12 or 24 Weeks	Males 3 to < 6 Years Old - SOF+RBV 12 or 24 Weeks	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	31	11	3	
Units: participants				
End of Treatment - No Change (N = 31, 11, 3)	24	11	3	
End of Treatment - Increase (N = 31, 11, 3)	7	0	0	
End of Treatment - Decrease (N = 31, 11, 3)	0	0	0	
Posttreatment Week 12 - No Change (N = 30, 11, 3)	21	10	3	
Posttreatment Week 12 - Increase (N = 30, 11, 3)	9	1	0	
Posttreatment Week 12 - Decrease (N = 30, 11, 3)	0	0	0	
Posttreatment Week 24 - No Change (N = 31, 11, 3)	20	9	3	
Posttreatment Week 24 - Increase (N = 31, 11, 3)	11	2	0	
Posttreatment Week 24 - Decrease (N = 31, 11, 3)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: For the Treatment Phase, Number of Female Participants With a Change From Baseline in Tanner Stage for Pubic Hair

End point title	For the Treatment Phase, Number of Female Participants With a Change From Baseline in Tanner Stage for Pubic Hair

End point description:

Tanner Stages is a scale that defines physical measurements of development based on external primary and secondary sex characteristics. It was used in this study to assess pubertal development with values ranging from Stage 1 (pre-pubertal characteristics) to Stage 5 (adult or mature characteristics). Any shifts (increase or decrease) in Tanner Stage from Baseline were analyzed and presented. Female participants in the Safety Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; End of Treatment (either Week 12 or 24), Posttreatment Week 12, and Posttreatment Week 24

End point values	Females 12 to < 18 Years Old - SOF+RBV 12 or 24 Weeks	Females 6 to < 12 Years Old - SOF+RBV 12 or 24 Weeks	Females 3 to < 6 Years Old - SOF+RBV 12 or 24 Weeks	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	21	30	8	
Units: participants				
End of Treatment - No Change (N = 21, 30, 8)	20	24	8	
End of Treatment - Increase (N = 21, 30, 8)	1	6	0	
End of Treatment - Decrease (N = 21, 30, 8)	0	0	0	
Posttreatment Week 12 - No Change (N = 20, 29, 8)	18	23	8	
Posttreatment Week 12 - Increase (N = 20, 29, 8)	2	6	0	
Posttreatment Week 12 - Decrease (N = 20, 29, 8)	0	0	0	
Posttreatment Week 24 - No Change (N = 20, 30, 8)	18	22	8	
Posttreatment Week 24 - Increase (N = 20, 30, 8)	2	8	0	
Posttreatment Week 24 - Decrease (N = 20, 30, 8)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: For the Treatment Phase, Number of Female Participants With a Change From Baseline in Tanner Stage for Breast Development

End point title	For the Treatment Phase, Number of Female Participants With a Change From Baseline in Tanner Stage for Breast Development

End point description:

Tanner Stages is a scale that defines physical measurements of development based on external primary and secondary sex characteristics. It was used in this study to assess pubertal development with values ranging from Stage 1 (pre-pubertal
characteristics) to Stage 5 (adult or mature characteristics). Any shifts (increase or decrease) in Tanner Stage from Baseline were analyzed and presented. Female participants in the Safety Analysis Set with

available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; End of Treatment (either Week 12 or 24), Posttreatment Week 12, and Posttreatment Week 24

End point values	Females 12 to < 18 Years Old - SOF+RBV 12 or 24 Weeks	Females 6 to < 12 Years Old - SOF+RBV 12 or 24 Weeks	Females 3 to < 6 Years Old - SOF+RBV 12 or 24 Weeks	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	21	30	8	
Units: participants				
End of Treatment - No Change (N = 21, 30, 8)	20	24	8	
End of Treatment - Increase (N = 21, 30, 8)	1	5	0	
End of Treatment - Decrease (N = 21, 30, 8)	0	1	0	
Posttreatment Week 12 - No Change (N = 20, 29, 8)	17	24	8	
Posttreatment Week 12 - Increase (N = 20, 29, 8)	3	5	0	
Posttreatment Week 12 - Decrease (N = 20, 29, 8)	0	0	0	
Posttreatment Week 24 - No Change (N = 20, 30, 8)	16	19	8	
Posttreatment Week 24 - Increase (N = 20, 30, 8)	4	11	0	
Posttreatment Week 24 - Decrease (N = 20, 30, 8)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: For the Treatment Phase, Palatability of SOF Granules at Day 1 as Assessed by the Percentage of Participants Able/ Unable to Taste the SOF Oral Granules

End point title	For the Treatment Phase, Palatability of SOF Granules at Day 1 as Assessed by the Percentage of Participants Able/ Unable to Taste the SOF Oral Granules

End point description:

Participants were asked if they were able to taste the SOF oral granules. Participants in the Safety Analysis Set who performed the palatability assessment were analyzed.

End point type	Secondary

End point timeframe:

Day 1

End point values	12 to < 18 Years Old - SOF+RBV 12 or 24 Weeks	6 to < 12 Years Old - SOF+RBV 12 or 24 Weeks	3 to < 6 Years Old - SOF+RBV 12 or 24 Weeks	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1	7	12	
Units: percentage of participants				
number (not applicable)				
Able to Taste SOF Granules: Yes	0	42.9	75.0	
Able to Taste SOF Granules: No	100.0	57.1	25.0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events: Up to 12 or 24 weeks (depending on group) plus 30 days; All-Cause Mortality: Up to Posttreatment Week 24

Adverse event reporting additional description:

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

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	12 to < 18 Years Old - SOF+RBV 12 Weeks

Reporting group description:

Participants 12 to < 18 years of age with HCV genotype 2 received SOF 400 mg (1 x 400 mg tablet, 4 x 100 mg tablets, or 8 x 50 mg oral granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 12 weeks.

Reporting group title	12 to < 18 Years Old - SOF+RBV 24 Weeks

Reporting group description:

Participants 12 to < 18 years of age with HCV genotype 3 received SOF 400 mg (1 x 400 mg tablet, 4 x 100 mg tablets, or 8 x 50 mg oral granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 24 weeks.

Reporting group title	6 to < 12 Years Old - SOF+RBV 12 Weeks

Reporting group description:

Participants 6 to < 12 years of age with HCV genotype 2 received SOF 200 mg (2 x 100 mg tablets or 4 x 50 mg oral granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 12 weeks.

Reporting group title	6 to < 12 Years Old - SOF+RBV 24 Weeks

Reporting group description:

Participants 6 to < 12 years of age with HCV genotype 3 received SOF 200 mg (2 x 100 mg tablets or 4 x 50 mg oral granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 24 weeks.

Reporting group title	3 to < 6 Years Old - SOF+RBV 12 Weeks

Reporting group description:

Participants 3 to < 6 years of age with HCV genotype 2 received SOF (weight ≥ 17 kg: 200 mg granules; weight < 17 kg: 150 mg granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 12 weeks.

Reporting group title	3 to < 6 Years Old - SOF+RBV 24 Weeks

Reporting group description:

Participants 3 to < 6 years of age with HCV genotype 3 received SOF (weight ≥ 17 kg: 200 mg granules; weight < 17 kg: 150 mg granules) once daily + RBV capsules or oral solution (up to 1400 mg, dose depending on weight) for 24 weeks.

Serious adverse events	12 to < 18 Years Old - SOF+RBV 12 Weeks	12 to < 18 Years Old - SOF+RBV 24 Weeks	6 to < 12 Years Old - SOF+RBV 12 Weeks
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	0 / 13 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	6 to < 12 Years Old - SOF+RBV 24 Weeks	3 to < 6 Years Old - SOF+RBV 12 Weeks	3 to < 6 Years Old - SOF+RBV 24 Weeks
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
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	12 to < 18 Years Old - SOF+RBV 12 Weeks	12 to < 18 Years Old - SOF+RBV 24 Weeks	6 to < 12 Years Old - SOF+RBV 12 Weeks
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 13 (92.31%)	27 / 39 (69.23%)	9 / 13 (69.23%)
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	1 / 13 (7.69%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 13 (0.00%)	4 / 39 (10.26%)	3 / 13 (23.08%)
occurrences (all)	0	6	3
Asthenia			
subjects affected / exposed	1 / 13 (7.69%)	5 / 39 (12.82%)	1 / 13 (7.69%)
occurrences (all)	1	6	2
Pyrexia			

subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 13 (0.00%)	2 / 39 (5.13%)	0 / 13 (0.00%)
occurrences (all)	0	3	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 13 (0.00%)	3 / 39 (7.69%)	1 / 13 (7.69%)
occurrences (all)	0	4	1
Oropharyngeal pain			
subjects affected / exposed	0 / 13 (0.00%)	4 / 39 (10.26%)	0 / 13 (0.00%)
occurrences (all)	0	4	0
Rhinorrhoea			
subjects affected / exposed	1 / 13 (7.69%)	2 / 39 (5.13%)	1 / 13 (7.69%)
occurrences (all)	1	2	1
Epistaxis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 39 (2.56%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Sinus congestion			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Pharyngeal erythema			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract congestion			

subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 39 (2.56%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Irritability			
subjects affected / exposed	1 / 13 (7.69%)	0 / 39 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Mood swings			
subjects affected / exposed	0 / 13 (0.00%)	2 / 39 (5.13%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Middle insomnia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Product issues			
Product taste abnormal			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Investigations			
Weight decreased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 39 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Cardiac murmur			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 13 (0.00%)	1 / 39 (2.56%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Arthropod bite			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0

Fall			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Scratch			
subjects affected / exposed	1 / 13 (7.69%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Ligament injury			
subjects affected / exposed	1 / 13 (7.69%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Product use issue			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Road traffic accident			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 13 (23.08%)	9 / 39 (23.08%)	4 / 13 (30.77%)
occurrences (all)	5	16	4
Dizziness			
subjects affected / exposed	0 / 13 (0.00%)	4 / 39 (10.26%)	0 / 13 (0.00%)
occurrences (all)	0	4	0
Migraine			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	1 / 13 (7.69%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 13 (0.00%)	1 / 39 (2.56%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Motion sickness			

subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 13 (7.69%)	3 / 39 (7.69%)	2 / 13 (15.38%)
occurrences (all)	1	3	3
Nausea			
subjects affected / exposed	3 / 13 (23.08%)	11 / 39 (28.21%)	0 / 13 (0.00%)
occurrences (all)	4	13	0
Diarrhoea			
subjects affected / exposed	2 / 13 (15.38%)	1 / 39 (2.56%)	1 / 13 (7.69%)
occurrences (all)	3	1	1
Abdominal pain upper			
subjects affected / exposed	2 / 13 (15.38%)	2 / 39 (5.13%)	1 / 13 (7.69%)
occurrences (all)	2	2	1
Abdominal pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 13 (0.00%)	3 / 39 (7.69%)	0 / 13 (0.00%)
occurrences (all)	0	3	0
Toothache			
subjects affected / exposed	0 / 13 (0.00%)	1 / 39 (2.56%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Mouth ulceration			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Anal pruritus			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Epigastric discomfort			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 13 (7.69%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0

Oral contusion			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Tooth loss			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 13 (7.69%)	3 / 39 (7.69%)	0 / 13 (0.00%)
occurrences (all)	1	3	0
Pruritus			
subjects affected / exposed	1 / 13 (7.69%)	1 / 39 (2.56%)	1 / 13 (7.69%)
occurrences (all)	1	1	1
Alopecia			
subjects affected / exposed	0 / 13 (0.00%)	2 / 39 (5.13%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Acne			
subjects affected / exposed	1 / 13 (7.69%)	1 / 39 (2.56%)	0 / 13 (0.00%)
occurrences (all)	1	1	0
Skin exfoliation			
subjects affected / exposed	0 / 13 (0.00%)	2 / 39 (5.13%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Erythema			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Rash papular			
subjects affected / exposed	1 / 13 (7.69%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 13 (0.00%)	1 / 39 (2.56%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Arthralgia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			

subjects affected / exposed	1 / 13 (7.69%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	1 / 13 (7.69%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Muscular weakness			
subjects affected / exposed	1 / 13 (7.69%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 13 (0.00%)	3 / 39 (7.69%)	1 / 13 (7.69%)
occurrences (all)	0	5	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 13 (0.00%)	2 / 39 (5.13%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Oral herpes			
subjects affected / exposed	1 / 13 (7.69%)	2 / 39 (5.13%)	0 / 13 (0.00%)
occurrences (all)	1	2	0
Ear infection			
subjects affected / exposed	0 / 13 (0.00%)	2 / 39 (5.13%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Gastroenteritis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Impetigo			
subjects affected / exposed	0 / 13 (0.00%)	2 / 39 (5.13%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Influenza			
subjects affected / exposed	0 / 13 (0.00%)	2 / 39 (5.13%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Rhinitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 39 (2.56%)	0 / 13 (0.00%)
occurrences (all)	0	1	0

Respiratory tract infection viral			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Tinea infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 39 (2.56%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	1 / 13 (7.69%)	1 / 39 (2.56%)	0 / 13 (0.00%)
occurrences (all)	1	1	0
Conjunctivitis viral			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Fungal skin infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Pharyngitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 39 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 13 (7.69%)	2 / 39 (5.13%)	2 / 13 (15.38%)
occurrences (all)	1	3	2

Non-serious adverse events	6 to < 12 Years Old - SOF+RBV 24 Weeks	3 to < 6 Years Old - SOF+RBV 12 Weeks	3 to < 6 Years Old - SOF+RBV 24 Weeks
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 28 (85.71%)	5 / 5 (100.00%)	8 / 8 (100.00%)
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed	5 / 28 (17.86%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	5	1	1
Asthenia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	4 / 28 (14.29%)	1 / 5 (20.00%)	0 / 8 (0.00%)
occurrences (all)	9	2	0
Influenza like illness			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Malaise			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 28 (0.00%)	1 / 5 (20.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 28 (25.00%)	1 / 5 (20.00%)	0 / 8 (0.00%)
occurrences (all)	9	1	0
Oropharyngeal pain			
subjects affected / exposed	4 / 28 (14.29%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	5	0	1
Rhinorrhoea			
subjects affected / exposed	3 / 28 (10.71%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	3	0	1
Epistaxis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Sinus congestion			

subjects affected / exposed	2 / 28 (7.14%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Pharyngeal erythema			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Upper respiratory tract congestion			
subjects affected / exposed	0 / 28 (0.00%)	1 / 5 (20.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Irritability			
subjects affected / exposed	0 / 28 (0.00%)	1 / 5 (20.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Mood swings			
subjects affected / exposed	1 / 28 (3.57%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Middle insomnia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 5 (20.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Product issues			
Product taste abnormal			
subjects affected / exposed	1 / 28 (3.57%)	1 / 5 (20.00%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Investigations			
Weight decreased			
subjects affected / exposed	1 / 28 (3.57%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Cardiac murmur			
subjects affected / exposed	1 / 28 (3.57%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			

Contusion			
subjects affected / exposed	3 / 28 (10.71%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Arthropod bite			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	2
Fall			
subjects affected / exposed	1 / 28 (3.57%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Scratch			
subjects affected / exposed	1 / 28 (3.57%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Ligament injury			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Product use issue			
subjects affected / exposed	0 / 28 (0.00%)	1 / 5 (20.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Road traffic accident			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 28 (28.57%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	25	0	0
Dizziness			
subjects affected / exposed	1 / 28 (3.57%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Migraine			
subjects affected / exposed	2 / 28 (7.14%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	10	0	0
Presyncope			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			

Lymphadenopathy			
subjects affected / exposed	2 / 28 (7.14%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 28 (3.57%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Motion sickness			
subjects affected / exposed	1 / 28 (3.57%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	4	0	1
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	11 / 28 (39.29%)	3 / 5 (60.00%)	3 / 8 (37.50%)
occurrences (all)	16	4	4
Nausea			
subjects affected / exposed	4 / 28 (14.29%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	4	0	1
Diarrhoea			
subjects affected / exposed	3 / 28 (10.71%)	2 / 5 (40.00%)	3 / 8 (37.50%)
occurrences (all)	4	2	4
Abdominal pain upper			
subjects affected / exposed	0 / 28 (0.00%)	1 / 5 (20.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	3 / 28 (10.71%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	1 / 28 (3.57%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Mouth ulceration			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Anal pruritus			

subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Epigastric discomfort			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Oral contusion			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Tooth loss			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	2 / 28 (7.14%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Pruritus			
subjects affected / exposed	1 / 28 (3.57%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Alopecia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 5 (20.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Acne			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Skin exfoliation			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Rash papular			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	2 / 28 (7.14%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Arthralgia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Muscle spasms			
subjects affected / exposed	1 / 28 (3.57%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Joint swelling			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 28 (14.29%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	4	0	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 28 (7.14%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	2	0	1
Oral herpes			
subjects affected / exposed	1 / 28 (3.57%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Ear infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	3 / 28 (10.71%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Impetigo			

subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Influenza			
subjects affected / exposed	1 / 28 (3.57%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	2 / 28 (7.14%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Respiratory tract infection viral			
subjects affected / exposed	1 / 28 (3.57%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Tinea infection			
subjects affected / exposed	0 / 28 (0.00%)	1 / 5 (20.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis viral			
subjects affected / exposed	0 / 28 (0.00%)	1 / 5 (20.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Folliculitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Fungal skin infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 28 (7.14%)	0 / 5 (0.00%)	3 / 8 (37.50%)
occurrences (all)	2	0	4

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 February 2014	• Specified that subjects must be treatment naive for the PK lead-in phase • Specified that subjects rolling over from the PK lead-in phase would not be required to perform laboratory assessments on Day 1 of the treatment phase • Included the protocol number (GS-US-334-1113) for the long-term follow-up study • Added coagulation testing to Day 7 of the PK lead-in phase • Specified that subjects would be administered a dosing diary with instructions for the PK lead-in phase • Removed SVR24 from the subgroup analyses • Added creatine kinase as a laboratory assessment • Added additional information regarding the development of SOF oral granular formulation • Specified that the subject and/or legal guardian would be asked at screening if the subject was able to swallow and tolerate taking pills • Added information regarding the SOF swallowability assessment on Day 1 of the PK lead-in phase or the treatment phase (as applicable) • Identified the PedsQL™ Pediatric Quality of Life Inventory V4.0 Short Form (SF15) as the Quality of Life survey instrument • Made additional administrative updates
14 March 2014	• Added RBV dosing to the PK lead-in phase • Specified that subjects rolling over from the PK lead-in phase would not be required to perform screening, Day 1, or Week 1 visits in the treatment phase • Added REBETOL® as an RBV study drug and updated the weight-based dosing to reflect the approved dosing criteria • Moved efficacy from a primary endpoint to a secondary endpoint • Removed the Quality of Life survey as a secondary endpoint • Clarified the safety endpoint and added historical SVR12 comparison • Clarified that the swallowability assessment would be performed with a placebo tablet to assess ability to swallow the 400 mg or 100 mg SOF tablet and specified that it would occur from screening up to the Day 1 visit • Added placebo tablet description and handling • Added bone age assessment as part of the safety assessment • Added virologic breakthrough futility assessment • Added inclusion criteria for treatment-experienced subjects • Modified the inclusion criteria for hemoglobin with levels for males ≥ 12 g/dL and females ≥ 11 g/dL • Added exclusion criteria for the glomerular filtration rate to be < 90 mL/min/1.73m^2 as calculated by the Schwartz Formula, and added the Schwartz Formula • Added dose reduction guidance of RBV per the REBETOL prescribing information • Added laboratory assessment of amylase
10 October 2014	• Added India to study center countries • Clarified the breakthrough futility assessment to specify that further enrollment would be suspended if 3 or more of the first 10 subjects enrolled had viral breakthrough at or prior to Week 8 • Added SOF oral granule formulation/packaging information as well as a palatability assessment • Included bioavailability data of SOF oral granules from Study GS-US-334-1111 • Revised the table for RBV dose administration by weight to allow participants whose body weight is ≥ 47 kg to receive oral ribavirin doses • Revised the SOF 400 mg pill count to be either 30 or 28 tablets per bottle • Clarified that subjects who did not attain SVR24 will also be enrolled in the separate GS-US-334-1113 protocol • Added clarification for pregnancy counseling of subjects < 12 years of age • Added parental height to medical history • Made additional administrative changes

12 November 2014	• Added language to clarify the reconsent requirement for subjects who became adults while on the study • Updated the RBV dosing chart to reflect accurate dosing of RBV for subjects ≥ 47 kg who may have utilized the RBV oral solution • Clarified that Gilead Sciences (Gilead), not the sites, would calculate the height/weight percentiles according to the Centers for Disease Control and Prevention (CDC) reference charts •Updated the statistical analysis secondary endpoint language to include previously omitted palatability assessment of SOF oral granules • Made additional administrative changes
29 May 2015	• Weight restrictions for Cohort 2 were added based on the Cohort 1 data analysis • The dose for Cohort 2 was added based on the Cohort 1 data analysis • Clarified the contraception language in the exclusion criteria • Updated statistical methods to align with regulatory requirements • Updated the table for dosage and administration of RBV to clarify the body weight range of 66 to 80 kgs (145 to 176 lbs) • Made additional administrative changes
26 February 2016	• The dose for Cohort 3 was added based on the Cohort 2 data analysis • Updated PK and safety results • Removed the collection and analysis of age of first menses • Clarified the glomerular filtration rate calculation • Made additional administrative changes

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/28543053

http://www.ncbi.nlm.nih.gov/pubmed/29193603