Clinical trial results:
A Phase 2, Open-Label, Multicenter, Multi-cohort Study to Investigate the Safety and Efficacy of Ledipasvir/Sofosbuvir Fixed Dose Combination +/- Ribavirin in Adolescents and Children with Chronic HCV-Infection

Summary

EudraCT number	2014-003578-17
Trial protocol	Outside EU/EEA GB
Global end of trial date	24 August 2018

Results information

Result version number	v1 (current)
This version publication date	03 March 2019
First version publication date	03 March 2019

Trial information

Trial identification

Sponsor protocol code	GS-US-337-1116

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02249182
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-001411-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	24 August 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 June 2018
Global end of trial reached?	Yes
Global end of trial date	24 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the PK Lead-in Phase of the study is to evaluate the steady state pharmacokinetics (PK) and confirm the dose of ledipasvir/sofobuvir (LDV/SOF) fixed dose combination (FDC) in hepatitis C virus (HCV)-infected pediatric participants. The PK Lead-in Phase will also evaluate the safety, tolerability, and antiviral activity of 10 days of dosing of LDV/SOF FDC in HCV-infected pediatric participants. The Treatment Phase will be initiated by age cohort after confirmation of age-appropriate LDV/SOF FDC dosage levels. Participants from the PK Lead-in Phase will immediately rollover into the Treatment Phase with no interruption of study drug administration.

The primary objective of the Treatment Phase is to evaluate the antiviral efficacy, safety, and tolerability of LDV/SOF FDC +/- ribavirin (RBV) for 12 or 24 weeks in pediatric participants with HCV.

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	05 November 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: 15
Country: Number of subjects enrolled	New Zealand: 4
Country: Number of subjects enrolled	Australia: 17
Country: Number of subjects enrolled	United States: 190
Worldwide total number of subjects	226
EEA total number of subjects	15

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)	126
Adolescents (12-17 years)	100
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 the United States, United Kingdom, Australia, and New Zealand. The first participant was screened on 05 November 2014. The last study visit occurred on 24 August 2018.

Pre-assignment

Screening details:

240 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 - LDV/SOF 12 Weeks

Arm description:

Participants 12 to < 18 years of age with HCV genotype 1 treatment-naive (TN) with or without cirrhosis or treatment-experienced (TE) without cirrhosis received LDV/SOF FDC 90/400 mg (1 x 90/400 mg tablet or 4 x 22.5/100 mg tablets) once daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Ledipasvir/sofosbuvir
Investigational medicinal product code	
Other name	LDV/SOF, Harvoni®, GS-5885/GS-7977
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

90/400 mg (1 x 90/400 mg tablet or 4 x 22.5/100 mg tablets) once daily

Arm title	6 to < 12 Years Old - LDV/SOF 12 Weeks

Arm description:

Participants 6 to < 12 years of age with HCV genotypes 1 or 4 TN with or without cirrhosis or HCV genotype 1 TE without cirrhosis received LDV/SOF FDC 45/200 mg (2 x 22.5/100 mg tablets or 4 x 11.25/50 mg granules) once daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Ledipasvir/sofosbuvir
Investigational medicinal product code	
Other name	LDV/SOF, Harvoni®, GS-5885/GS-7977
Pharmaceutical forms	Tablet, Granules
Routes of administration	Oral use

Dosage and administration details:

45/200 mg (2 x 22.5/100 mg tablets or 4 x 11.25/50 mg granules) once daily

Arm title	6 to < 12 Years Old - LDV/SOF 24 Weeks

Arm description:

Participants 6 to < 12 years of age with HCV genotype 1 TE with cirrhosis received LDV/SOF FDC 45/200 mg (2 x 22.5/100 mg tablets or 4 x 11.25/50 mg granules) once daily for 24 weeks.

Arm type	Experimental

Investigational medicinal product name	Ledipasvir/sofosbuvir
Investigational medicinal product code	
Other name	LDV/SOF, Harvoni®, GS-5885/GS-7977
Pharmaceutical forms	Granules, Tablet
Routes of administration	Oral use

Dosage and administration details:

45/200 mg (2 x 22.5/100 mg tablets or 4 x 11.25/50 mg granules) once daily

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

Arm description:

Participants 6 to < 12 years of age with HCV genotype 3 TE without cirrhosis received LDV/SOF FDC 45/200 mg (2 x 22.5/100 mg tablets or 4 x 11.25/50 mg granules) once daily + ribavirin capsules or oral solution (dose depending on weight) for 24 weeks.

Note: Participants with cirrhosis could have enrolled in this age group, but none were actually enrolled. Only participants in the United Kingdom were enrolled in this group.

Arm type	Experimental
Investigational medicinal product name	Ledipasvir/sofosbuvir
Investigational medicinal product code	
Other name	LDV/SOF, Harvoni®, GS-5885/GS-7977
Pharmaceutical forms	Granules, Tablet
Routes of administration	Oral use

Dosage and administration details:

45/200 mg (2 x 22.5/100 mg tablets or 4 x 11.25/50 mg 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:

Administered orally in a divided daily dose based on weight

Arm title	3 to < 6 Years Old - LDV/SOF 12 Weeks

Arm description:

Participants 3 to < 6 years of age with HCV genotypes 1 or 4 TN without cirrhosis received LDV/SOF FDC (weight ≥ 17 kg: 45/200 mg granules; weight < 17 kg: 33.75/150 mg granules) once daily for 12 weeks.
Note: Participants with cirrhosis could have enrolled in this age group, but none were actually enrolled.

Arm type	Experimental
Investigational medicinal product name	Ledipasvir/sofosbuvir
Investigational medicinal product code	
Other name	LDV/SOF, Harvoni®, GS-5885/GS-7977
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

LDV/SOF (weight ≥ 17 kg: 45/200 mg granules; weight < 17 kg: 33.75/150 mg granules) once daily

Number of subjects in period 1	12 to < 18 Years Old - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 24 Weeks
Started	100	89	1
Completed	96	89	1
Not completed	4	0	0
Lost to follow-up	4	-	-

Number of subjects in period 1	6 to < 12 Years Old - LDV/SOF+RBV 24 Weeks	3 to < 6 Years Old - LDV/SOF 12 Weeks
Started	2	34
Completed	2	34
Not completed	0	0
Lost to follow-up	-	-

Baseline characteristics

Reporting groups	
Reporting group title	12 to < 18 Years Old - LDV/SOF 12 Weeks
Reporting group description:	
Participants 12 to < 18 years of age with HCV genotype 1 treatment-naive (TN) with or without cirrhosis or treatment-experienced (TE) without cirrhosis received LDV/SOF FDC 90/400 mg (1 x 90/400 mg tablet or 4 x 22.5/100 mg tablets) once daily for 12 weeks.	
Reporting group title	6 to < 12 Years Old - LDV/SOF 12 Weeks
Reporting group description:	
Participants 6 to < 12 years of age with HCV genotypes 1 or 4 TN with or without cirrhosis or HCV genotype 1 TE without cirrhosis received LDV/SOF FDC 45/200 mg (2 x 22.5/100 mg tablets or 4 x 11.25/50 mg granules) once daily for 12 weeks.	
Reporting group title	6 to < 12 Years Old - LDV/SOF 24 Weeks
Reporting group description:	
Participants 6 to < 12 years of age with HCV genotype 1 TE with cirrhosis received LDV/SOF FDC 45/200 mg (2 x 22.5/100 mg tablets or 4 x 11.25/50 mg granules) once daily for 24 weeks.	
Reporting group title	6 to < 12 Years Old - LDV/SOF+RBV 24 Weeks
Reporting group description:	
Participants 6 to < 12 years of age with HCV genotype 3 TE without cirrhosis received LDV/SOF FDC 45/200 mg (2 x 22.5/100 mg tablets or 4 x 11.25/50 mg granules) once daily + ribavirin capsules or oral solution (dose depending on weight) for 24 weeks. Note: Participants with cirrhosis could have enrolled in this age group, but none were actually enrolled. Only participants in the United Kingdom were enrolled in this group.	
Reporting group title	3 to < 6 Years Old - LDV/SOF 12 Weeks
Reporting group description:	
Participants 3 to < 6 years of age with HCV genotypes 1 or 4 TN without cirrhosis received LDV/SOF FDC (weight ≥ 17 kg: 45/200 mg granules; weight < 17 kg: 33.75/150 mg granules) once daily for 12 weeks. Note: Participants with cirrhosis could have enrolled in this age group, but none were actually enrolled.	

Reporting group values	12 to < 18 Years Old - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 24 Weeks
Number of subjects	100	89	1
Age categorical Units: Subjects			
Age continuous			
999 = NA; Standard deviation of a single sample is undefined.			
Units: years			
arithmetic mean	15	9	11
standard deviation	± 1.7	± 1.6	± 999
Gender categorical Units: Subjects			
Female	63	36	1
Male	37	53	0
Race Units: Subjects			
White	91	70	1
Black or African American	7	7	0
Other	0	5	0

Asian	2	5	0
Native Hawaiian or Pacific Islander	0	2	0
Ethnicity Units: Subjects			
Hispanic or Latino	13	9	0
Not Hispanic or Latino	85	75	1
Not Disclosed	2	5	0
HCV Genotype Units: Subjects			
Genotype 1	100	87	1
Genotype 3	0	0	0
Genotype 4	0	2	0
Cirrhosis Status Units: Subjects			
Yes	1	1	1
No	43	33	0
Unknown	56	55	0
IL28b Status			
The CC, CT, and TT alleles are different forms of the IL28b gene.			
Units: Subjects			
CC	24	23	0
CT	53	53	0
TT	23	12	1
Missing	0	1	0
HCV RNA Category Units: Subjects			
< 800,000 IU/mL	45	37	0
≥ 800,000 IU/mL	55	52	1
Prior Treatment Experience Units: Subjects			
Treatment-Naive	80	72	0
Treatment-Experienced	20	17	1

Reporting group values	6 to < 12 Years Old - LDV/SOF+RBV 24 Weeks	3 to < 6 Years Old - LDV/SOF 12 Weeks	Total
Number of subjects	2	34	226
Age categorical Units: Subjects			
Age continuous			
999 = NA; Standard deviation of a single sample is undefined.			
Units: years			
arithmetic mean	9	4	
standard deviation	± 2.8	± 0.7	-
Gender categorical Units: Subjects			
Female	1	24	125
Male	1	10	101
Race Units: Subjects			
White	2	27	191

Black or African American	0	1	15
Other	0	4	9
Asian	0	2	9
Native Hawaiian or Pacific Islander	0	0	2
Ethnicity Units: Subjects			
Hispanic or Latino	0	6	28
Not Hispanic or Latino	2	28	191
Not Disclosed	0	0	7
HCV Genotype Units: Subjects			
Genotype 1	0	33	221
Genotype 3	2	0	2
Genotype 4	0	1	3
Cirrhosis Status Units: Subjects			
Yes	0	0	3
No	2	14	92
Unknown	0	20	131
IL28b Status			
The CC, CT, and TT alleles are different forms of the IL28b gene.			
Units: Subjects			
CC	0	10	57
CT	2	16	124
TT	0	6	42
Missing	0	2	3
HCV RNA Category Units: Subjects			
< 800,000 IU/mL	1	15	98
≥ 800,000 IU/mL	1	19	128
Prior Treatment Experience Units: Subjects			
Treatment-Naive	0	34	186
Treatment-Experienced	2	0	40

End points

End points reporting groups

Reporting group title	12 to < 18 Years Old - LDV/SOF 12 Weeks

Reporting group description:

Participants 12 to < 18 years of age with HCV genotype 1 treatment-naive (TN) with or without cirrhosis or treatment-experienced (TE) without cirrhosis received LDV/SOF FDC 90/400 mg (1 x 90/400 mg tablet or 4 x 22.5/100 mg tablets) once daily for 12 weeks.

Reporting group title	6 to < 12 Years Old - LDV/SOF 12 Weeks

Reporting group description:

Participants 6 to < 12 years of age with HCV genotypes 1 or 4 TN with or without cirrhosis or HCV genotype 1 TE without cirrhosis received LDV/SOF FDC 45/200 mg (2 x 22.5/100 mg tablets or 4 x 11.25/50 mg granules) once daily for 12 weeks.

Reporting group title	6 to < 12 Years Old - LDV/SOF 24 Weeks

Reporting group description:

Participants 6 to < 12 years of age with HCV genotype 1 TE with cirrhosis received LDV/SOF FDC 45/200 mg (2 x 22.5/100 mg tablets or 4 x 11.25/50 mg granules) once daily for 24 weeks.

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

Reporting group description:

Participants 6 to < 12 years of age with HCV genotype 3 TE without cirrhosis received LDV/SOF FDC 45/200 mg (2 x 22.5/100 mg tablets or 4 x 11.25/50 mg granules) once daily + ribavirin capsules or oral solution (dose depending on weight) for 24 weeks.

Note: Participants with cirrhosis could have enrolled in this age group, but none were actually enrolled. Only participants in the United Kingdom were enrolled in this group.

Reporting group title	3 to < 6 Years Old - LDV/SOF 12 Weeks

Reporting group description:

Participants 3 to < 6 years of age with HCV genotypes 1 or 4 TN without cirrhosis received LDV/SOF FDC (weight ≥ 17 kg: 45/200 mg granules; weight < 17 kg: 33.75/150 mg granules) once daily for 12 weeks.
Note: Participants with cirrhosis could have enrolled in this age group, but none were actually enrolled.

Subject analysis set title	12 to < 18 Years Old - LDV/SOF 12 Weeks (PK Lead-in)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants 12 to < 18 years of age received LDV/SOF FDC 90/400 mg (1 x 90/400 mg tablet or 4 x 22.5/100 mg tablets) once daily for 12 weeks. 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.

Subject analysis set title	6 to < 12 Years Old - LDV/SOF 12 Weeks (PK Lead-in)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants 6 to < 12 years of age received LDV/SOF FDC 45/200 mg (2 x 22.5/100 mg tablets or 4 x 11.25/50 mg granules) once daily for 12 weeks. 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.

Subject analysis set title	3 to < 6 Years Old - LDV/SOF 12 Weeks (PK Lead-in)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants 3 to < 6 years of age received LDV/SOF FDC (weight ≥ 17 kg: 45/200 mg granules; weight < 17 kg: 33.75/150 mg granules) once daily for 12 weeks. 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.

Subject analysis set title	Males 12 to < 18 Years Old - LDV/SOF 12 Weeks
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Male participants 12 to < 18 years of age received LDV/SOF FDC 90/400 mg (1 x 90/400 mg tablet or 4

x 22.5/100 mg tablets) once daily for 12 weeks.

Subject analysis set title	Males 6 to < 12 Years Old - LDV/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 LDV/SOF FDC 45/200 mg (2 x 22.5/100 mg tablets or 4 x 11.25/50 mg granules) once daily ± RBV capsules or oral solution (dose depending on weight) for 12 or 24 weeks.

Subject analysis set title	Males 3 to < 6 Years Old - LDV/SOF 12 Weeks
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Male participants 3 to < 6 years of age received LDV/SOF FDC (weight ≥ 17 kg: 45/200 mg granules; weight < 17 kg: 33.75/150 mg granules) once daily for 12 weeks.

Subject analysis set title	Females 12 to < 18 Years Old - LDV/SOF 12 Weeks
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Female participants 12 to < 18 years of age received LDV/SOF FDC 90/400 mg (1 x 90/400 mg tablet or 4 x 22.5/100 mg tablets) once daily for 12 weeks.

Subject analysis set title	Females 6 to < 12 Years Old - LDV/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 LDV/SOF FDC 45/200 mg (2 x 22.5/100 mg tablets or 4 x 11.25/50 mg granules) once daily ± RBV capsules or oral solution (dose depending on weight) for 12 or 24 weeks.

Subject analysis set title	Females 3 to < 6 Years Old - LDV/SOF 12 Weeks
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Female participants 3 to < 6 years of age received LDV/SOF FDC (weight ≥ 17 kg: 45/200 mg granules; weight < 17 kg: 33.75/150 mg granules) once daily for 12 weeks.

Subject analysis set title	12 to < 18 Years Old - LDV/SOF 12 Weeks
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants 12 to < 18 years of age received LDV/SOF FDC 90/400 mg (1 x 90/400 mg tablet or 4 x 22.5/100 mg tablets) once daily for 12 weeks.

Subject analysis set title	6 to < 12 Years Old - LDV/SOF±RBV 12 or 24 Weeks
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants 6 to < 12 years of age received LDV/SOF FDC 45/200 mg (2 x 22.5/100 mg tablets or 4 x 11.25/50 mg granules) once daily ± RBV capsules or oral solution (dose depending on weight) for 12 or 24 weeks.

Subject analysis set title	3 to < 6 Years Old - LDV/SOF 12 Weeks
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants 3 to < 6 years of age received LDV/SOF FDC (weight ≥ 17 kg: 45/200 mg granules; weight < 17 kg: 33.75/150 mg granules) once daily for 12 weeks.

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

End point title	For Participants in the PK Lead-in Phase, PK Parameter: AUCtau of GS-331007, LDV, and SOF[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:

Cohorts 1 and 2 (6 to < 18 years of age): predose, 0.5, 1, 2, 3, 4, 5, 8, and 12 hours postdose on Day 10; Cohort 3 (3 to < 6 years of age): predose, 0.5, 2, 4, 8, and 12 hours postdose on Day 10

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, LDV, and SOF for each age group in the PK Lead-in Phase 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	12 to < 18 Years Old - LDV/SOF 12 Weeks (PK Lead-in)	6 to < 12 Years Old - LDV/SOF 12 Weeks (PK Lead-in)	3 to < 6 Years Old - LDV/SOF 12 Weeks (PK Lead-in)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	10	13	
Units: h*ng/mL				
arithmetic mean (standard deviation)				
GS-331007 (N = 10, 10, 13)	12682.5 (± 1732.66)	8210.3 (± 2542.42)	11688.9 (± 3400.79)	
LDV (N = 10, 10, 13)	10202.4 (± 5196.49)	7288.3 (± 4547.33)	9316.3 (± 3280.51)	
SOF (N = 10, 9, 3)	2175.7 (± 578.92)	1754.4 (± 419.18)	2495.2 (± 412.64)	

Attachments (see zip file)	Statistical Analysis/337-1116_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 were enrolled into the study and received 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 - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 24 Weeks	6 to < 12 Years Old - LDV/SOF+RBV 24 Weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	89	1	2
Units: percentage of participants				
number (not applicable)	0	0	0	0

End point values	3 to < 6 Years Old - LDV/SOF 12 Weeks			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: percentage of participants				
number (not applicable)	2.9			

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.

End point type	Secondary

End point timeframe:

Baseline; Weeks 1, 2, 4, 8, and 12

End point values	12 to < 18 Years Old - LDV/SOF 12 Weeks (PK Lead-in)	6 to < 12 Years Old - LDV/SOF 12 Weeks (PK Lead-in)	3 to < 6 Years Old - LDV/SOF 12 Weeks (PK Lead-in)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	12	17	
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Change at Week 1 (N = 10, 12, 17)	-4.34 (± 0.621)	-4.29 (± 0.518)	-4.32 (± 0.616)	
Change at Week 2 (N = 10, 12, 15)	-4.71 (± 0.651)	-4.55 (± 0.636)	-4.87 (± 0.724)	
Change at Week 4 (N = 10, 12, 16)	-4.73 (± 0.667)	-4.75 (± 0.702)	-4.92 (± 0.715)	
Change at Week 8 (N = 10, 12, 16)	-4.73 (± 0.667)	-4.76 (± 0.710)	-4.92 (± 0.715)	

Change at Week 12 (N = 10, 12, 16)	-4.73 (± 0.667)	-4.76 (± 0.710)	-4.92 (± 0.715)	

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 10	

End point values	12 to < 18 Years Old - LDV/SOF 12 Weeks (PK Lead-in)	6 to < 12 Years Old - LDV/SOF 12 Weeks (PK Lead-in)	3 to < 6 Years Old - LDV/SOF 12 Weeks (PK Lead-in)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	12	17	
Units: percentage of participants				
number (not applicable)	0	0	5.9	

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 < the lower limit of quantitation (LLOQ; ie, 15 IU/mL) at 4 weeks after stopping study treatment. Full Analysis Set included all participants who were enrolled into the study and received at least 1 dose of study drug.	
End point type	Secondary
End point timeframe: Posttreatment Week 4	

End point values	12 to < 18 Years Old - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 24 Weeks	6 to < 12 Years Old - LDV/SOF+RBV 24 Weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	89	1	2
Units: percentage of participants				
number (confidence interval 95%)	98.0 (93.0 to 99.8)	98.9 (93.9 to 100.0)	100.0 (2.5 to 100.0)	100.0 (15.8 to 100.0)

End point values	3 to < 6 Years Old - LDV/SOF 12 Weeks			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: percentage of participants				
number (confidence interval 95%)	97.1 (84.7 to 99.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: 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)

End point description:

SVR12 was defined as HCV RNA < LLOQ at 12 weeks after stopping study treatment. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Posttreatment Week 12

End point values	12 to < 18 Years Old - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 24 Weeks	6 to < 12 Years Old - LDV/SOF+RBV 24 Weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	89	1	2
Units: percentage of participants				
number (confidence interval 95%)	98.0 (93.0 to 99.8)	98.9 (93.9 to 100.0)	100.0 (2.5 to 100.0)	100.0 (15.8 to 100.0)

End point values	3 to < 6 Years Old - LDV/SOF 12 Weeks			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: percentage of participants				
number (confidence interval 95%)	97.1 (84.7 to 99.9)			

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 - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 24 Weeks	6 to < 12 Years Old - LDV/SOF+RBV 24 Weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	89	1	2
Units: percentage of participants				
number (confidence interval 95%)	98.0 (93.0 to 99.8)	98.9 (93.9 to 100.0)	100.0 (2.5 to 100.0)	100.0 (15.8 to 100.0)

End point values	3 to < 6 Years Old - LDV/SOF 12 Weeks			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: percentage of participants				
number (confidence interval 95%)	97.1 (84.7 to 99.9)			

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 - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 24 Weeks	6 to < 12 Years Old - LDV/SOF+RBV 24 Weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	89	1	2
Units: percentage of participants				
number (not applicable)	0	0	0	0

End point values	3 to < 6 Years Old - LDV/SOF 12 Weeks			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: percentage of participants				
number (not applicable)	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 - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 24 Weeks	6 to < 12 Years Old - LDV/SOF+RBV 24 Weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	89	1	2
Units: percentage of participants				
number (not applicable)	0	1.1	0	0

End point values	3 to < 6 Years Old - LDV/SOF 12 Weeks			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: percentage of participants				
number (not applicable)	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. 9999 = NA; Standard deviation of a single sample is undefined.

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 - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 24 Weeks	6 to < 12 Years Old - LDV/SOF+RBV 24 Weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	89	1	2
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Change at Week 1 (N = 98, 85, 1, 2, 34)	-4.34 (± 0.634)	-4.27 (± 0.592)	-4.30 (± 9999)	-4.54 (± 0.308)
Change at Week 2 (N = 99, 88, 1, 2, 32)	-4.74 (± 0.585)	-4.73 (± 0.544)	-5.09 (± 9999)	-4.54 (± 0.308)
Change at Week 4 (N = 100, 89, 1, 2, 33)	-4.84 (± 0.557)	-4.87 (± 0.592)	-5.09 (± 9999)	-4.54 (± 0.308)
Change at Week 8 (N = 99, 89, 1, 2, 33)	-4.85 (± 0.556)	-4.89 (± 0.597)	-5.09 (± 9999)	-4.54 (± 0.308)
Change at Week 12 (N = 99, 89, 1, 2, 33)	-4.85 (± 0.556)	-4.89 (± 0.597)	-5.09 (± 9999)	-4.54 (± 0.308)
Change at Week 16 (N = NA, NA, 1, 2, NA)	999 (± 999)	999 (± 999)	-5.09 (± 9999)	-4.54 (± 0.308)
Change at Week 20 (N = NA, NA, 1, 2, NA)	999 (± 999)	999 (± 999)	-5.09 (± 9999)	-4.54 (± 0.308)
Change at Week 24 (N = NA, NA, 1, 2, NA)	999 (± 999)	999 (± 999)	-5.09 (± 9999)	-4.54 (± 0.308)

End point values	3 to < 6 Years Old - LDV/SOF 12 Weeks			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Change at Week 1 (N = 98, 85, 1, 2, 34)	-4.25 (± 0.505)			
Change at Week 2 (N = 99, 88, 1, 2, 32)	-4.80 (± 0.628)			
Change at Week 4 (N = 100, 89, 1, 2, 33)	-4.80 (± 0.628)			
Change at Week 8 (N = 99, 89, 1, 2, 33)	-4.86 (± 0.633)			
Change at Week 12 (N = 99, 89, 1, 2, 33)	-4.86 (± 0.633)			
Change at Week 16 (N = NA, NA, 1, 2, NA)	999 (± 999)			
Change at Week 20 (N = NA, NA, 1, 2, NA)	999 (± 999)			
Change at Week 24 (N = NA, NA, 1, 2, NA)	999 (± 999)			

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 - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 24 Weeks	6 to < 12 Years Old - LDV/SOF+RBV 24 Weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	89	1	2
Units: percentage of participants				
number (confidence interval 95%)				
Week 1 (N = 100, 89, 1, 2, 34)	40.0 (30.3 to 50.3)	30.3 (21.0 to 41.0)	0 (0.0 to 97.5)	100.0 (15.8 to 100.0)
Week 2 (N = 100, 89, 1, 2, 33)	75.0 (65.3 to 83.1)	71.9 (61.4 to 80.9)	100.0 (2.5 to 100.0)	100.0 (15.8 to 100.0)
Week 4 (N = 100, 89, 1, 2, 33)	97.0 (91.5 to 99.4)	96.6 (90.5 to 99.3)	100.0 (2.5 to 100.0)	100.0 (15.8 to 100.0)
Week 8 (N = 99, 89, 1, 2, 33)	100.0 (96.3 to 100.0)	100.0 (95.9 to 100.0)	100.0 (2.5 to 100.0)	100.0 (15.8 to 100.0)
Week 12 (N = 99, 89, 1, 2, 33)	100.0 (96.3 to 100.0)	100.0 (95.9 to 100.0)	100.0 (2.5 to 100.0)	100.0 (15.8 to 100.0)
Week 16 (N = NA, NA, 1, 2, NA)	9999 (999 to 99999)	9999 (999 to 99999)	100.0 (2.5 to 100.0)	100.0 (15.8 to 100.0)
Week 20 (N = NA, NA, 1, 2, NA)	9999 (999 to 99999)	9999 (999 to 99999)	100.0 (2.5 to 100.0)	100.0 (15.8 to 100.0)
Week 24 (N = NA, NA, 1, 2, NA)	9999 (999 to 99999)	9999 (999 to 99999)	100.0 (2.5 to 100.0)	100.0 (15.8 to 100.0)

End point values	3 to < 6 Years Old - LDV/SOF 12 Weeks			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: percentage of participants				
number (confidence interval 95%)				
Week 1 (N = 100, 89, 1, 2, 34)	29.4 (15.1 to 47.5)			
Week 2 (N = 100, 89, 1, 2, 33)	78.8 (61.1 to 91.0)			
Week 4 (N = 100, 89, 1, 2, 33)	97.0 (84.2 to 99.9)			
Week 8 (N = 99, 89, 1, 2, 33)	100.0 (89.4 to 100.0)			

Week 12 (N = 99, 89, 1, 2, 33)	100.0 (89.4 to 100.0)			
Week 16 (N = NA, NA, 1, 2, NA)	9999 (999 to 99999)			
Week 20 (N = NA, NA, 1, 2, NA)	9999 (999 to 99999)			
Week 24 (N = NA, NA, 1, 2, NA)	9999 (999 to 99999)			

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. 999 = Not Applicable; Participants in the Full Analysis Set with ALT > ULN at Baseline with available data were analyzed. 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 - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 24 Weeks	6 to < 12 Years Old - LDV/SOF+RBV 24 Weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	72	1	2
Units: percentage of participants				
number (not applicable)				
Week 1 (N = 47, 70, 1, 2, 27)	72.3	75.7	0	50.0
Week 2 (N = 49, 66, 1, 2, 25)	89.8	84.8	0	50.0
Week 4 (N = 48, 72, 1, 2, 25)	93.8	93.1	0	100.0
Week 8 (N = 46, 71, 1, 2, 25)	91.3	90.1	0	100.0
Week 12 (N = 45, 67, 1, 2, 24)	93.3	95.5	100.0	100.0
Week 16 (N = NA, NA, 1, 2, NA)	999	999	100.0	100.0
Week 20 (N = NA, NA, 1, 2, NA)	999	999	100.0	100.0
Week 24 (N = NA, NA, 1, 2, NA)	999	999	100.0	100.0
Posttreatment Week 4 (N = 41, 62, 0, 2, 23)	90.2	98.4	999	100.0

End point values	3 to < 6 Years Old - LDV/SOF			

	12 Weeks			
Subject group type	Reporting group			
Number of subjects analysed	27			
Units: percentage of participants				
number (not applicable)				
Week 1 (N = 47, 70, 1, 2, 27)	63.0			
Week 2 (N = 49, 66, 1, 2, 25)	84.0			
Week 4 (N = 48, 72, 1, 2, 25)	96.0			
Week 8 (N = 46, 71, 1, 2, 25)	92.0			
Week 12 (N = 45, 67, 1, 2, 24)	91.7			
Week 16 (N = NA, NA, 1, 2, NA)	999			
Week 20 (N = NA, NA, 1, 2, NA)	999			
Week 24 (N = NA, NA, 1, 2, NA)	999			
Posttreatment Week 4 (N = 41, 62, 0, 2, 23)	91.3			

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. 9999 = NA; Standard deviation of a single sample is undefined.

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 - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 24 Weeks	6 to < 12 Years Old - LDV/SOF+RBV 24 Weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	89	1	2
Units: centimeters				
arithmetic mean (standard deviation)				
Change at Week 1 (N = 97, 85, 1, 2, 34)	0.1 (± 0.68)	0.1 (± 0.83)	0.3 (± 9999)	0.7 (± 1.13)
Change at Week 2 (N = 97, 86, 1, 2, 32)	0.0 (± 0.70)	0.3 (± 0.73)	0.5 (± 9999)	0.5 (± 0.85)
Change at Week 4 (N = 98, 87, 1, 2, 33)	0.1 (± 0.84)	0.5 (± 0.79)	1.2 (± 9999)	0.6 (± 0.92)
Change at Week 8 (N = 98, 88, 1, 2, 33)	0.4 (± 1.04)	0.8 (± 0.79)	1.3 (± 9999)	0.8 (± 0.92)
Change at Week 12 (N = 92, 84, 1, 2, 31)	0.5 (± 1.10)	1.3 (± 0.83)	2.1 (± 9999)	1.1 (± 1.41)

Change at Week 16 (N = NA, NA, 1, 2, NA)	999 (± 999)	999 (± 999)	3.2 (± 9999)	1.4 (± 1.06)
Change at Week 20 (N = NA, NA, 1, 2, NA)	999 (± 999)	999 (± 999)	4.3 (± 9999)	1.6 (± 0.85)
Change at Week 24 (N = NA, NA, 1, 2, NA)	999 (± 999)	999 (± 999)	4.3 (± 9999)	2.5 (± 1.48)
Change at PT Wk 4 (N = 97, 89, 1, 2, 34)	0.8 (± 1.46)	1.8 (± 1.04)	4.3 (± 9999)	2.4 (± 1.27)
Change at PT Wk 12 (N = 96, 87, 1, 2, 34)	1.2 (± 1.82)	2.7 (± 0.97)	5.0 (± 9999)	3.4 (± 1.56)
Change at PT Wk 24 (N = 95, 88, 1, 2, 34)	1.8 (± 2.31)	4.1 (± 1.39)	7.6 (± 9999)	5.6 (± 0.85)

End point values	3 to < 6 Years Old - LDV/SOF 12 Weeks			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: centimeters				
arithmetic mean (standard deviation)				
Change at Week 1 (N = 97, 85, 1, 2, 34)	0.2 (± 1.24)			
Change at Week 2 (N = 97, 86, 1, 2, 32)	0.3 (± 0.72)			
Change at Week 4 (N = 98, 87, 1, 2, 33)	0.7 (± 0.79)			
Change at Week 8 (N = 98, 88, 1, 2, 33)	1.0 (± 0.82)			
Change at Week 12 (N = 92, 84, 1, 2, 31)	1.6 (± 0.98)			
Change at Week 16 (N = NA, NA, 1, 2, NA)	999 (± 999)			
Change at Week 20 (N = NA, NA, 1, 2, NA)	999 (± 999)			
Change at Week 24 (N = NA, NA, 1, 2, NA)	999 (± 999)			
Change at PT Wk 4 (N = 97, 89, 1, 2, 34)	2.1 (± 1.13)			
Change at PT Wk 12 (N = 96, 87, 1, 2, 34)	3.3 (± 1.18)			
Change at PT Wk 24 (N = 95, 88, 1, 2, 34)	4.7 (± 1.31)			

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. 9999 = NA; Standard deviation of a single sample is undefined.

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 - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 24 Weeks	6 to < 12 Years Old - LDV/SOF+RBV 24 Weeks
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	89	1	2
Units: kilograms				
arithmetic mean (standard deviation)				
Change at Week 1 (N = 98, 86, 1, 2, 34)	0.1 (± 1.00)	0.3 (± 0.51)	-0.5 (± 9999)	0.3 (± 1.34)
Change at Week 2 (N = 97, 87, 1, 2, 33)	0.3 (± 1.11)	0.4 (± 0.54)	0.0 (± 9999)	0.3 (± 1.77)
Change at Week 4 (N = 98, 89, 1, 2, 33)	0.4 (± 1.44)	0.5 (± 0.64)	0.5 (± 9999)	0.7 (± 1.91)
Change at Week 8 (N = 98, 89, 1, 2, 33)	0.5 (± 1.90)	0.8 (± 0.84)	1.3 (± 9999)	0.6 (± 2.33)
Change at Week 12 (N = 92, 84, 1, 2, 31)	0.6 (± 2.32)	1.1 (± 1.27)	2.1 (± 9999)	0.9 (± 2.90)
Change at Week 16 (N = NA, NA, 1, 2, NA)	999 (± 999)	999 (± 999)	1.6 (± 9999)	1.2 (± 3.68)
Change at Week 20 (N = NA, NA, 1, 2, NA)	999 (± 999)	999 (± 999)	2.2 (± 9999)	1.8 (± 3.96)
Change at Week 24 (N = NA, NA, 1, 2, NA)	999 (± 999)	999 (± 999)	3.1 (± 9999)	2.4 (± 3.68)
Change at PT Wk 4 (N = 97, 89, 1, 2, 34)	0.9 (± 2.70)	1.4 (± 1.48)	1.8 (± 9999)	2.2 (± 3.68)
Change at PT Wk 12 (N = 96, 89, 1, 2, 34)	1.6 (± 3.48)	2.1 (± 1.87)	3.1 (± 9999)	3.7 (± 2.90)
Change at PT Wk 24 (N = 95, 89, 1, 2, 34)	3.2 (± 4.38)	3.5 (± 2.75)	4.5 (± 9999)	5.7 (± 1.41)

End point values	3 to < 6 Years Old - LDV/SOF 12 Weeks			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: kilograms				
arithmetic mean (standard deviation)				
Change at Week 1 (N = 98, 86, 1, 2, 34)	0.1 (± 0.39)			
Change at Week 2 (N = 97, 87, 1, 2, 33)	0.2 (± 0.44)			
Change at Week 4 (N = 98, 89, 1, 2, 33)	0.3 (± 0.64)			
Change at Week 8 (N = 98, 89, 1, 2, 33)	0.5 (± 0.66)			
Change at Week 12 (N = 92, 84, 1, 2, 31)	0.6 (± 0.70)			

Change at Week 16 (N = NA, NA, 1, 2, NA)	999 (± 999)			
Change at Week 20 (N = NA, NA, 1, 2, NA)	999 (± 999)			
Change at Week 24 (N = NA, NA, 1, 2, NA)	999 (± 999)			
Change at PT Wk 4 (N = 97, 89, 1, 2, 34)	1.1 (± 1.09)			
Change at PT Wk 12 (N = 96, 89, 1, 2, 34)	1.2 (± 0.93)			
Change at PT Wk 24 (N = 95, 89, 1, 2, 34)	2.0 (± 1.57)			

Statistical analyses

No statistical analyses for this end point

Secondary: Acceptability of LDV/SOF Tablets as Measured by the Percentage of Participants Able/ Unable to Swallow Placebo Tablet at Day 1

End point title	Acceptability of LDV/SOF Tablets as Measured by the Percentage of Participants Able/ Unable to Swallow Placebo Tablet at Day 1

End point description:

Participants who were able/unable to swallow placebo tablets were assessed. Participants 12 to < 18 years old were first asked to perform the swallowability assessment using the 90/400 mg placebo tablet. If they were unable to swallow this, they were then asked to perform the swallowability assessment with 22.5/100 mg placebo tablets. Participants 6 to < 12 years old were to be assessed with the 22.5/100 mg placebo tablets. However, 8 participants were mistakenly assessed using the 90/400 mg placebo tablet.

Participants between 6 to <18 years old in the Safety Analysis Set who performed the swallowability assessment were analyzed.

End point type	Secondary

End point timeframe:

Day 1

End point values	12 to < 18 Years Old - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF±RBV 12 or 24 Weeks		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	100	92		
Units: percentage of participants				
number (not applicable)				
Able to Swallow 90/400 mg Tablet (N = 100, 8)	89.0	100.0		
Unable to Swallow 90/400 mg Tablet (N = 100, 8)	11.0	0		
Able to Swallow 22.5/100 mg Tablet (N = 11, 84)	72.7	98.8		
Unable to Swallow 22.5/100 mg Tablet (N = 11, 84)	27.3	1.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Acceptability of LDV/SOF Granules as Measured by Palatability at Day 1

End point title	Acceptability of LDV/SOF Granules as Measured by Palatability at Day 1

End point description:

Participants who were dosed with granules were asked if they tasted the study drug. If they tasted it, then they were asked to provide a number from 0 to 100 to rate the taste of the study drug, with higher scores indicating better taste. Data was then summarized as percentage of participants choosing the following palatability categories: 1) Did not taste the study drug, 2) Tasted drug with score > 60 to 100, 3) Tasted drug with score 40 to 60, and 4) Tasted drug with score of 0 to < 40. Participants between 3 to <6 years old in the Safety Analysis Set who performed the palatability test were analyzed.

End point type	Secondary

End point timeframe:

Day 1

End point values	3 to < 6 Years Old - LDV/SOF 12 Weeks			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: percentage of participants				
number (not applicable)				
Did not taste the study drug	41.2			
Tasted drug with score > 60 to 100	17.6			
Tasted drug with score 40 to 60	11.8			
Tasted drug with score of 0 to < 40	29.4			

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.

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 - LDV/SOF 12 Weeks	Males 6 to < 12 Years Old - LDV/SOF± RBV 12 or 24 Weeks	Males 3 to < 6 Years Old - LDV/SOF 12 Weeks	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	37	54	10	
Units: participants				
End of Treatment - No Change (N = 36, 54, 10)	35	52	10	
End of Treatment - Increase (N = 36, 54, 10)	1	1	0	
End of Treatment - Decrease (N = 36, 54, 10)	0	1	0	
Posttreatment Week 12 - No Change (N = 35, 54, 9)	32	51	9	
Posttreatment Week 12 - Increase (N = 35, 54, 9)	3	2	0	
Posttreatment Week 12 - Decrease (N = 35, 54, 9)	0	1	0	
Posttreatment Week 24 - No Change (N = 35, 53, 10)	28	48	9	
Posttreatment Week 24 - Increase (N = 35, 53, 10)	7	4	1	
Posttreatment Week 24 - Decrease (N = 35, 53, 10)	0	1	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.

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 - LDV/SOF 12 Weeks	Males 6 to < 12 Years Old - LDV/SOF± RBV 12 or 24 Weeks	Males 3 to < 6 Years Old - LDV/SOF 12 Weeks	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	37	54	10	
Units: participants				
End of Treatment - No Change (N = 35, 54, 10)	34	52	10	
End of Treatment - Increase (N = 35, 54, 10)	1	1	0	
End of Treatment - Decrease (N = 35, 54, 10)	0	1	0	
Posttreatment Week 12 - No Change (N = 35, 54, 9)	33	50	9	
Posttreatment Week 12 - Increase (N = 35, 54, 9)	2	4	0	
Posttreatment Week 12 - Decrease (N = 35, 54, 9)	0	0	0	
Posttreatment Week 24 - No Change (N = 35, 53, 10)	29	47	10	
Posttreatment Week 24 - Increase (N = 35, 53, 10)	6	6	0	
Posttreatment Week 24 - Decrease (N = 35, 53, 10)	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.

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 - LDV/SOF 12 Weeks	Females 6 to < 12 Years Old - LDV/SOF± RBV 12 or 24 Weeks	Females 3 to < 6 Years Old - LDV/SOF 12 Weeks	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	63	38	24	
Units: participants				
End of Treatment - No Change (N = 62, 36, 21)	52	34	21	
End of Treatment - Increase (N = 62, 36, 21)	9	2	0	
End of Treatment - Decrease (N = 62, 36, 21)	1	0	0	
Posttreatment Week 12 - No Change (N = 60, 34, 22)	45	31	22	
Posttreatment Week 12 - Increase (N = 60, 34, 22)	15	3	0	
Posttreatment Week 12 - Decrease (N = 60, 34, 22)	0	0	0	
Posttreatment Week 24 - No Change (N = 61, 35, 22)	40	27	22	
Posttreatment Week 24 - Increase (N = 61, 35, 22)	21	8	0	
Posttreatment Week 24 - Decrease (N = 61, 35, 22)	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.

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 - LDV/SOF 12 Weeks	Females 6 to < 12 Years Old - LDV/SOF± RBV 12 or 24 Weeks	Females 3 to < 6 Years Old - LDV/SOF 12 Weeks	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	63	38	24	
Units: participants				
End of Treatment - No Change (N = 62, 36, 21)	53	31	21	
End of Treatment - Increase (N = 62, 36, 21)	8	5	0	
End of Treatment - Decrease (N = 62, 36, 21)	1	0	0	
Posttreatment Week 12 - No Change (N = 60, 34, 22)	49	25	21	
Posttreatment Week 12 - Increase (N = 60, 34, 22)	11	8	1	
Posttreatment Week 12 - Decrease (N = 60, 34, 22)	0	1	0	
Posttreatment Week 24 - No Change (N = 61, 35, 22)	43	21	21	
Posttreatment Week 24 - Increase (N = 61, 35, 22)	18	14	1	
Posttreatment Week 24 - Decrease (N = 61, 35, 22)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 12 or 24 weeks (depending on group) plus 30 days

Adverse event reporting additional description:

Safety Analysis Set included all participants who were enrolled into the study and received 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 - LDV/SOF 12 Weeks

Reporting group description:

Participants 12 to < 18 years of age with HCV genotype 1 TN with or without cirrhosis or HCV genotype 1 TE without cirrhosis received LDV/SOF FDC 90/400 mg (1 x 90/400 mg tablet or 4 x 22.5/100 mg tablets) once daily for 12 weeks.

Reporting group title	6 to < 12 Years Old - LDV/SOF 12 Weeks

Reporting group description:

Participants 6 to < 12 years of age with HCV genotypes 1 or 4 TN with or without cirrhosis or HCV genotype 1 TE without cirrhosis received LDV/SOF FDC 45/200 mg (2 x 22.5/100 mg tablets or 4 x 11.25/50 mg granules) once daily for 12 weeks.

Reporting group title	6 to < 12 Years Old - LDV/SOF 24 Weeks

Reporting group description:

Participants 6 to < 12 years of age with HCV genotype 1 TE with cirrhosis received LDV/SOF FDC 45/200 mg (2 x 22.5/100 mg tablets or 4 x 11.25/50 mg granules) once daily for 24 weeks.

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

Reporting group description:

Participants 6 to < 12 years of age with HCV genotype 3 TE without cirrhosis received LDV/SOF FDC 45/200 mg (2 x 22.5/100 mg tablets or 4 x 11.25/50 mg granules) once daily + ribavirin capsules or oral solution (dose depending on weight) for 24 weeks.

Note: Participants with cirrhosis could have enrolled in this age group, but none were actually enrolled. Only participants in the United Kingdom were enrolled in this group.

Reporting group title	3 to < 6 Years Old - LDV/SOF 12 Weeks

Reporting group description:

Participants 3 to < 6 years of age with HCV genotypes 1 or 4 TN without cirrhosis received LDV/SOF FDC (weight ≥ 17 kg: 45/200 mg granules; weight < 17 kg: 33.75/150 mg granules) once daily for 12 weeks.
Note: Participants with cirrhosis could have enrolled in this age group, but none were actually enrolled.

Serious adverse events	12 to < 18 Years Old - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 24 Weeks
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 100 (0.00%)	1 / 89 (1.12%)	0 / 1 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 100 (0.00%)	1 / 89 (1.12%)	0 / 1 (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
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 100 (0.00%)	1 / 89 (1.12%)	0 / 1 (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
Tooth abscess			
subjects affected / exposed	0 / 100 (0.00%)	1 / 89 (1.12%)	0 / 1 (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

Serious adverse events	6 to < 12 Years Old - LDV/SOF+RBV 24 Weeks	3 to < 6 Years Old - LDV/SOF 12 Weeks	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	0 / 34 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth abscess			
subjects affected / exposed	0 / 2 (0.00%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	12 to < 18 Years Old - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 12 Weeks	6 to < 12 Years Old - LDV/SOF 24 Weeks
Total subjects affected by non-serious adverse events			
subjects affected / exposed	62 / 100 (62.00%)	54 / 89 (60.67%)	1 / 1 (100.00%)
Injury, poisoning and procedural complications			
Skin abrasion			
subjects affected / exposed	1 / 100 (1.00%)	1 / 89 (1.12%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Fall			
subjects affected / exposed	0 / 100 (0.00%)	1 / 89 (1.12%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	26 / 100 (26.00%)	16 / 89 (17.98%)	0 / 1 (0.00%)
occurrences (all)	41	19	0
Dizziness			
subjects affected / exposed	2 / 100 (2.00%)	5 / 89 (5.62%)	0 / 1 (0.00%)
occurrences (all)	3	5	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	13 / 100 (13.00%)	13 / 89 (14.61%)	0 / 1 (0.00%)
occurrences (all)	13	14	0
Pyrexia			
subjects affected / exposed	2 / 100 (2.00%)	15 / 89 (16.85%)	0 / 1 (0.00%)
occurrences (all)	2	17	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 100 (0.00%)	2 / 89 (2.25%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	12 / 100 (12.00%)	12 / 89 (13.48%)	0 / 1 (0.00%)
occurrences (all)	14	12	0
Diarrhoea			

subjects affected / exposed	13 / 100 (13.00%)	11 / 89 (12.36%)	0 / 1 (0.00%)
occurrences (all)	15	13	0
Abdominal pain			
subjects affected / exposed	7 / 100 (7.00%)	14 / 89 (15.73%)	0 / 1 (0.00%)
occurrences (all)	8	14	0
Nausea			
subjects affected / exposed	11 / 100 (11.00%)	9 / 89 (10.11%)	0 / 1 (0.00%)
occurrences (all)	15	9	0
Abdominal pain upper			
subjects affected / exposed	7 / 100 (7.00%)	3 / 89 (3.37%)	0 / 1 (0.00%)
occurrences (all)	7	3	0
Mouth ulceration			
subjects affected / exposed	0 / 100 (0.00%)	2 / 89 (2.25%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	5 / 100 (5.00%)	0 / 89 (0.00%)	0 / 1 (0.00%)
occurrences (all)	6	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	10 / 100 (10.00%)	11 / 89 (12.36%)	1 / 1 (100.00%)
occurrences (all)	11	12	3
Oropharyngeal pain			
subjects affected / exposed	10 / 100 (10.00%)	10 / 89 (11.24%)	0 / 1 (0.00%)
occurrences (all)	10	10	0
Nasal congestion			
subjects affected / exposed	6 / 100 (6.00%)	5 / 89 (5.62%)	1 / 1 (100.00%)
occurrences (all)	7	5	1
Rhinorrhoea			
subjects affected / exposed	2 / 100 (2.00%)	3 / 89 (3.37%)	1 / 1 (100.00%)
occurrences (all)	2	3	1
Epistaxis			
subjects affected / exposed	2 / 100 (2.00%)	2 / 89 (2.25%)	1 / 1 (100.00%)
occurrences (all)	2	2	1
Skin and subcutaneous tissue disorders			

Rash			
subjects affected / exposed	1 / 100 (1.00%)	8 / 89 (8.99%)	0 / 1 (0.00%)
occurrences (all)	1	8	0
Dermatitis contact			
subjects affected / exposed	4 / 100 (4.00%)	0 / 89 (0.00%)	0 / 1 (0.00%)
occurrences (all)	6	0	0
Ecchymosis			
subjects affected / exposed	2 / 100 (2.00%)	0 / 89 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Dermatitis allergic			
subjects affected / exposed	0 / 100 (0.00%)	0 / 89 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 100 (0.00%)	0 / 89 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin odour abnormal			
subjects affected / exposed	0 / 100 (0.00%)	0 / 89 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 100 (1.00%)	1 / 89 (1.12%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	5 / 100 (5.00%)	3 / 89 (3.37%)	0 / 1 (0.00%)
occurrences (all)	5	3	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	5 / 100 (5.00%)	7 / 89 (7.87%)	0 / 1 (0.00%)
occurrences (all)	6	7	0
Nasopharyngitis			
subjects affected / exposed	7 / 100 (7.00%)	2 / 89 (2.25%)	0 / 1 (0.00%)
occurrences (all)	8	2	0
Pharyngitis streptococcal			
subjects affected / exposed	0 / 100 (0.00%)	3 / 89 (3.37%)	0 / 1 (0.00%)
occurrences (all)	0	4	0

Conjunctivitis			
subjects affected / exposed	0 / 100 (0.00%)	1 / 89 (1.12%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Ear infection			
subjects affected / exposed	0 / 100 (0.00%)	0 / 89 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Product issues			
Product taste abnormal			
subjects affected / exposed	0 / 100 (0.00%)	0 / 89 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	6 to < 12 Years Old - LDV/SOF+RBV 24 Weeks	3 to < 6 Years Old - LDV/SOF 12 Weeks	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	22 / 34 (64.71%)	
Injury, poisoning and procedural complications			
Skin abrasion			
subjects affected / exposed	0 / 2 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Fall			
subjects affected / exposed	1 / 2 (50.00%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 2 (50.00%)	3 / 34 (8.82%)	
occurrences (all)	1	3	
Dizziness			
subjects affected / exposed	0 / 2 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 2 (50.00%)	2 / 34 (5.88%)	
occurrences (all)	2	2	
Pyrexia			
subjects affected / exposed	1 / 2 (50.00%)	7 / 34 (20.59%)	
occurrences (all)	2	11	
Ear and labyrinth disorders			

Ear pain			
subjects affected / exposed	1 / 2 (50.00%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 2 (50.00%)	8 / 34 (23.53%)	
occurrences (all)	2	10	
Diarrhoea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 34 (0.00%)	
occurrences (all)	0	0	
Abdominal pain			
subjects affected / exposed	0 / 2 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Nausea			
subjects affected / exposed	1 / 2 (50.00%)	1 / 34 (2.94%)	
occurrences (all)	1	1	
Abdominal pain upper			
subjects affected / exposed	0 / 2 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Mouth ulceration			
subjects affected / exposed	1 / 2 (50.00%)	1 / 34 (2.94%)	
occurrences (all)	1	2	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 34 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 2 (50.00%)	7 / 34 (20.59%)	
occurrences (all)	1	8	
Oropharyngeal pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Nasal congestion			
subjects affected / exposed	0 / 2 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	3	

Rhinorrhoea			
subjects affected / exposed	0 / 2 (0.00%)	6 / 34 (17.65%)	
occurrences (all)	0	8	
Epistaxis			
subjects affected / exposed	0 / 2 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 2 (0.00%)	3 / 34 (8.82%)	
occurrences (all)	0	3	
Dermatitis contact			
subjects affected / exposed	0 / 2 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Ecchymosis			
subjects affected / exposed	0 / 2 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	3	
Dermatitis allergic			
subjects affected / exposed	1 / 2 (50.00%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Rash maculo-papular			
subjects affected / exposed	1 / 2 (50.00%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Skin odour abnormal			
subjects affected / exposed	1 / 2 (50.00%)	0 / 34 (0.00%)	
occurrences (all)	2	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 2 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 34 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Upper respiratory tract infection			

subjects affected / exposed	0 / 2 (0.00%)	3 / 34 (8.82%)	
occurrences (all)	0	4	
Nasopharyngitis			
subjects affected / exposed	1 / 2 (50.00%)	1 / 34 (2.94%)	
occurrences (all)	2	2	
Pharyngitis streptococcal			
subjects affected / exposed	0 / 2 (0.00%)	4 / 34 (11.76%)	
occurrences (all)	0	4	
Conjunctivitis			
subjects affected / exposed	0 / 2 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Ear infection			
subjects affected / exposed	0 / 2 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Product issues			
Product taste abnormal			
subjects affected / exposed	0 / 2 (0.00%)	3 / 34 (8.82%)	
occurrences (all)	0	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 October 2014	• Removed Russia from the list of study site countries participating in the trial • Updated the futility rule to suspend enrollment if 3 or more of the first 10 subjects enrolled have viral breakthrough or are nonresponders at or prior to Week 8 • Included genotype 3 HCV infection as an exclusion criterion • Updated the formulation, packaging and labeling, and storage and handling information to include information on the lower dose strength tablet (LDV/SOF 22.5/100 mg and placebo-to-match). • Clarified that subjects who do not attain SVR24 will also be enrolled in the separate registry study (GS-US-334-1113). • Changed the growth and development measurements from a PK lead-in secondary endpoint to a treatment phase secondary endpoint. • Added clarification on pregnancy notification timelines for partners of male subjects participating in the trial. • Additional administrative updates were made.
08 December 2014	• The study design was updated to include a treatment period of 24 weeks with LDV/SOF for treatment-experienced subjects with cirrhosis, to comply with the approved US prescribing information. • Added clarification on the exclusion criteria (with a history of cirrhosis) for the PK lead-in phase • Additional statistical analysis was added to include analysis of the LDV/SOF 24-week treatment group (treatment-experienced subjects with cirrhosis) • Added language in the introduction to reflect the approval of LDV/SOF in the US and EU • Language added to clarify the reconsent requirement for subjects who become adults while on the study • Revised statistical endpoints to be consistent with the protocol objectives • Additional administrative, formatting, section number, and minor grammatical corrections and updates were made throughout the document.
28 May 2015	• The study design was updated to add treatment with LDV/SOF+RBV for 24 weeks for subjects with genotype 3 HCV infection, to comply with the approved UK prescribing information. • The study design was updated to reflect that subjects with genotypes 3 or 4 HCV infection would only be enrolled in the UK, to comply with the approved UK prescribing information. • The study design for the long-term follow-up study (GS-US-334-1113) was updated to reduce the number of visits, fulfilling the regulatory requirement minimum. • The statistical methods were updated to align with the updated treatment regimens. • New clinical data available for subjects with genotype 3 and 4 HCV infection were added to the introduction to reflect the approved UK prescribing information. • Added information on RBV to the introduction, investigational medicinal products section, and to the inclusion criteria • The exclusion criteria contraception language within the synopsis was updated to clarify the contraception requirements. • Amiodarone was been added to the disallowed agents list in the prior and concomitant medications section • Pregnancy tests and prevention requirements and RBV toxicity management were added for the subjects receiving RBV. • References for new clinical data and Tanner Stage Scale were added.

15 March 2016	• The study design was updated to include additional genotypes (genotypes 5 and 6) following the availability of supporting data within the adult population. Updates were also made to the background consistent with these changes. • The study procedures and statistical methods sections were updated to remove the collection and analysis of age of first menses. • Clarifications were made to the estimated glomerular filtration rate (eGFR) calculation. • Additional minor updates were made throughout the document.
04 November 2016	• Clarified that the swallowability assessment was not required for subjects receiving the oral granule formulation • Added information regarding oral granule formulation dosing, labeling, packaging, and storage specifications • Added new clinical data from a Phase 1 bioavailability study to the introduction to supportuse of the oral granule formulation • Updated the definition of a treatment-emergent adverse event (AE) as any AE with an onset date on or after the study drug start date and no later than 30 days after permanent discontinuation of the study drug or any AE leading to premature discontinuation of the study drug • Added additional HBV serological testing (ie, hepatitis B surface antibody [HBsAb], hepatitis B core antibody [HBcAb]) at screening and specified that serial hepatitis B virus (HBV) DNA monitoring should occur for any subjects who were HBcAb positive at screening
08 June 2017	• Updated the study design to increase the number of subjects from approximately 200 to approximately 220, including subjects in the PK lead-in phase: approximately 100 adolescent subjects 12 to < 18 years old and approximately 120 pediatric subjects 3 to < 12 years old • Added a palatability assessment for LDV/SOF oral granules at Day 1 for subjects 3 to < 6 years of age • Updated the study design to include an optional intensive PK substudy, to be completed at Week 4 or 8, for subjects 3 to < 12 years old who provided written consent

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/30070726

http://www.ncbi.nlm.nih.gov/pubmed/28957984

http://www.ncbi.nlm.nih.gov/pubmed/27997679