Clinical trial results:
A Two-Part, Open-Label, Single-Arm Phase 1/2 Study of Safety, Pharmacokinetics, and Efficacy of Telaprevir in Combination With Peginterferon alfa-2b and Ribavirin in Pediatric Subjects Aged 3 to 17 Infected With Genotype 1 Hepatitis C Virus

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2011-004564-30
Trial protocol	GB DE BE IT ES
Global end of trial date	07 April 2015

Results information

Result version number	v1 (current)
This version publication date	13 July 2016
First version publication date	13 July 2016

Trial information

Trial identification

Sponsor protocol code	VX11-950-118

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01701063
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Vertex Pharmaceuticals Incorporated
Sponsor organisation address	50 Northern Avenue, Boston, Massachusetts, United States, 02210-1862
Public contact	Medical Monitor, Vertex Pharmaceuticals Incorporated, +1 617341-6777, medicalinfo@vrtx.com
Scientific contact	Medical Monitor, Vertex Pharmaceuticals Incorporated, +1 617341-6777, medicalinfo@vrtx.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000196-PIP01-08
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	22 May 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 April 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

PART A
- To evaluate the short-term safety of telaprevir in combination with pegylated interferon (Peg-IFN) and ribavirin (RBV) (Peg-IFN/RBV) in treatment-naive pediatric subjects without cirrhosis.
- To evaluate the pharmacokinetics (PK) and determine the appropriate dose of telaprevir in combination with Peg-IFN/RBV in treatment-naive pediatric subjects without cirrhosis.

PART B
- To evaluate the safety of telaprevir in combination with Peg-IFN/RBV in treatment-naive and peginterferon/RBV treatment-experienced pediatric subjects with or without cirrhosis.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and the International Conference on Harmonization (ICH) Guideline for Good Clinical Practice (GCP).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 January 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	United States: 28
Worldwide total number of subjects	42
EEA total number of subjects	14

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)	25
Adolescents (12-17 years)	15
Adults (18-64 years)	2
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study was planned to be conducted in 2 parts (Part A and Part B), which would use separate groups of subjects. However, the study was
terminated early (12 weeks after last dose of study drug in Part A) and Part B was not conducted.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1 (13-17 Years): Telaprevir + Peg-IFN-alfa-2b + RBV

Arm description:

Subjects aged 13 to 17 years received telaprevir twice daily for 12 weeks either as a film coated tablet (15 milligram per kilogram [mg/kg] of body weight) or as a chewable tablet (14 mg/kg of body weight) in combination with pegylated interferon alfa 2b (Peg-IFN-alfa-2b) 60 microgram per meter square (mcg/m^2) subcutaneous injection weekly and ribavirin (RBV) 200 mg capsules or 40 milligram per milliliter (mg/mL) solution orally twice daily with a maximum dose of 1200 mg per day. Peg-IFN-alfa-2b and RBV were administered for 24 weeks in subjects who achieved extended rapid virologic response (eRVR) or for 48 weeks in subjects who did not achieve eRVR. eRVR was defined as undetectable hepatitis C virus ribonucleic acid (HCV RNA) levels at Week 4 and Week 12.

Arm type	Experimental
Investigational medicinal product name	Telaprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Chewable tablet, Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Telaprevir twice daily for 12 weeks either as a film coated tablet (15 mg/kg of body weight) or as a chewable tablet (14 mg/kg of body weight).

Investigational medicinal product name	Peg-IFN-alfa-2b
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Peg-IFN-alfa-2b 60 mcg/m^2 subcutaneous injection weekly for 24 weeks in subjects who achieved eRVR or for 48 weeks in subjects who did not achieve eRVR.

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

Dosage and administration details:

RBV 200 mg capsules or 40 mg/mL solution orally twice daily with a maximum dose of 1200 mg per day for 24 weeks in subjects who achieved eRVR or for 48 weeks in subjects who did not achieve eRVR.

Arm title	Cohort 2 (7-12 Years): Telaprevir + Peg-IFN-alfa-2b + RBV

Arm description:

Subjects aged 7 to 12 years received telaprevir twice daily for 12 weeks as a chewable tablet (16 mg/kg of body weight) in combination with Peg-IFN-alfa-2b 60 mcg/m^2 subcutaneous injection weekly and RBV 200-mg capsules or 40 mg/mL solution orally twice daily with a maximum dose of 1200 mg per day. Peg-IFN-alfa-2b and RBV were administered for 24 weeks in subjects who achieved eRVR or for 48 weeks in subjects who did not achieve eRVR. eRVR was defined as undetectable HCV RNA levels at Week 4 and Week 12.

Arm type	Experimental
Investigational medicinal product name	Telaprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

Telaprevir twice daily for 12 weeks as a chewable tablet (16 mg/kg of body weight)

Investigational medicinal product name	Peg-IFN-alfa-2b
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Peg-IFN-alfa-2b 60 mcg/m^2 subcutaneous injection weekly for 24 weeks in subjects who achieved eRVR or for 48 weeks in subjects who did not achieve eRVR.

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

Dosage and administration details:

RBV 200 mg capsules or 40 mg/mL solution orally twice daily with a maximum dose of 1200 mg per day for 24 weeks in subjects who achieved eRVR or for 48 weeks in subjects who did not achieve eRVR.

Arm title	Cohort 3 (3-6 Years): Telaprevir + Peg-IFN-alfa-2b + RBV

Arm description:

Subjects aged 3 to 6 years received telaprevir twice daily for 12 weeks as a chewable tablet (18 mg/kg of body weight) in combination with Peg-IFN-alfa-2b 60 mcg/m^2 subcutaneous injection weekly and RBV 200-mg capsules or 40 mg/mL solution orally twice daily with a maximum dose of 1200 mg per day. Peg-IFN-alfa-2b and RBV were administered for 24 weeks in subjects who achieved eRVR or for 48 weeks in subjects who did not achieve eRVR. eRVR was defined as undetectable HCV RNA levels at Week 4 and Week 12.

Arm type	Experimental
Investigational medicinal product name	Telaprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

Telaprevir twice daily for 12 weeks as a chewable tablet (18 mg/kg of body weight)

Investigational medicinal product name	Peg-IFN-alfa-2b
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Peg-IFN-alfa-2b 60 mcg/m^2 subcutaneous injection weekly for 24 weeks in subjects who achieved eRVR or for 48 weeks in subjects who did not achieve eRVR.

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

Dosage and administration details:

RBV 200 mg capsules or 40 mg/mL solution orally twice daily with a maximum dose of 1200 mg per day for 24 weeks in subjects who achieved eRVR or for 48 weeks in subjects who did not achieve eRVR.

Number of subjects in period 1	Cohort 1 (13-17 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 2 (7-12 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 3 (3-6 Years): Telaprevir + Peg-IFN-alfa-2b + RBV
Started	13	19	10
Completed	13	18	8
Not completed	0	1	2
Consent withdrawn by subject	-	-	1
Unspecified	-	-	1
Lost to follow-up	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1 (13-17 Years): Telaprevir + Peg-IFN-alfa-2b + RBV

Reporting group description:

Subjects aged 13 to 17 years received telaprevir twice daily for 12 weeks either as a film coated tablet (15 milligram per kilogram [mg/kg] of body weight) or as a chewable tablet (14 mg/kg of body weight) in combination with pegylated interferon alfa 2b (Peg-IFN-alfa-2b) 60 microgram per meter square (mcg/m^2) subcutaneous injection weekly and ribavirin (RBV) 200 mg capsules or 40 milligram per milliliter (mg/mL) solution orally twice daily with a maximum dose of 1200 mg per day. Peg-IFN-alfa-2b and RBV were administered for 24 weeks in subjects who achieved extended rapid virologic response (eRVR) or for 48 weeks in subjects who did not achieve eRVR. eRVR was defined as undetectable hepatitis C virus ribonucleic acid (HCV RNA) levels at Week 4 and Week 12.

Reporting group title	Cohort 2 (7-12 Years): Telaprevir + Peg-IFN-alfa-2b + RBV

Reporting group description:

Subjects aged 7 to 12 years received telaprevir twice daily for 12 weeks as a chewable tablet (16 mg/kg of body weight) in combination with Peg-IFN-alfa-2b 60 mcg/m^2 subcutaneous injection weekly and RBV 200-mg capsules or 40 mg/mL solution orally twice daily with a maximum dose of 1200 mg per day. Peg-IFN-alfa-2b and RBV were administered for 24 weeks in subjects who achieved eRVR or for 48 weeks in subjects who did not achieve eRVR. eRVR was defined as undetectable HCV RNA levels at Week 4 and Week 12.

Reporting group title	Cohort 3 (3-6 Years): Telaprevir + Peg-IFN-alfa-2b + RBV

Reporting group description:

Subjects aged 3 to 6 years received telaprevir twice daily for 12 weeks as a chewable tablet (18 mg/kg of body weight) in combination with Peg-IFN-alfa-2b 60 mcg/m^2 subcutaneous injection weekly and RBV 200-mg capsules or 40 mg/mL solution orally twice daily with a maximum dose of 1200 mg per day. Peg-IFN-alfa-2b and RBV were administered for 24 weeks in subjects who achieved eRVR or for 48 weeks in subjects who did not achieve eRVR. eRVR was defined as undetectable HCV RNA levels at Week 4 and Week 12.

Reporting group values	Cohort 1 (13-17 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 2 (7-12 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 3 (3-6 Years): Telaprevir + Peg-IFN-alfa-2b + RBV
Number of subjects	13	19	10
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	14.9	10.2	4.9
standard deviation	± 2.06	± 1.57	± 0.88
Gender categorical			
Units: Subjects			
Female	11	13	4
Male	2	6	6

Reporting group values	Total		
Number of subjects	42		
Age categorical			
Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	- 		
Gender categorical Units: Subjects			
Female	28		
Male	14		

End points

End points reporting groups

Reporting group title	Cohort 1 (13-17 Years): Telaprevir + Peg-IFN-alfa-2b + RBV

Reporting group description:

Subjects aged 13 to 17 years received telaprevir twice daily for 12 weeks either as a film coated tablet (15 milligram per kilogram [mg/kg] of body weight) or as a chewable tablet (14 mg/kg of body weight) in combination with pegylated interferon alfa 2b (Peg-IFN-alfa-2b) 60 microgram per meter square (mcg/m^2) subcutaneous injection weekly and ribavirin (RBV) 200 mg capsules or 40 milligram per milliliter (mg/mL) solution orally twice daily with a maximum dose of 1200 mg per day. Peg-IFN-alfa-2b and RBV were administered for 24 weeks in subjects who achieved extended rapid virologic response (eRVR) or for 48 weeks in subjects who did not achieve eRVR. eRVR was defined as undetectable hepatitis C virus ribonucleic acid (HCV RNA) levels at Week 4 and Week 12.

Reporting group title	Cohort 2 (7-12 Years): Telaprevir + Peg-IFN-alfa-2b + RBV

Reporting group description:

Subjects aged 7 to 12 years received telaprevir twice daily for 12 weeks as a chewable tablet (16 mg/kg of body weight) in combination with Peg-IFN-alfa-2b 60 mcg/m^2 subcutaneous injection weekly and RBV 200-mg capsules or 40 mg/mL solution orally twice daily with a maximum dose of 1200 mg per day. Peg-IFN-alfa-2b and RBV were administered for 24 weeks in subjects who achieved eRVR or for 48 weeks in subjects who did not achieve eRVR. eRVR was defined as undetectable HCV RNA levels at Week 4 and Week 12.

Reporting group title	Cohort 3 (3-6 Years): Telaprevir + Peg-IFN-alfa-2b + RBV

Reporting group description:

Subjects aged 3 to 6 years received telaprevir twice daily for 12 weeks as a chewable tablet (18 mg/kg of body weight) in combination with Peg-IFN-alfa-2b 60 mcg/m^2 subcutaneous injection weekly and RBV 200-mg capsules or 40 mg/mL solution orally twice daily with a maximum dose of 1200 mg per day. Peg-IFN-alfa-2b and RBV were administered for 24 weeks in subjects who achieved eRVR or for 48 weeks in subjects who did not achieve eRVR. eRVR was defined as undetectable HCV RNA levels at Week 4 and Week 12.

Subject analysis set title	Overall Subjects
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects aged 3 to 17 years received telaprevir twice daily for 12 weeks either as a film coated tablet (15 mg/kg of body weight) or as a chewable tablet (14 to 18 mg/kg of body weight) in combination with Peg-IFN-alfa-2b 60 mcg/m^2 subcutaneous injection weekly and RBV 200 mg capsules or 40 mg/mL solution orally twice daily with a maximum dose of 1200 mg per day. Peg-IFN-alfa-2b and RBV were administered for 24 weeks in subjects who achieved eRVR or for 48 weeks in subjects who did not achieve eRVR. eRVR was defined as undetectable HCV RNA levels at Week 4 and Week 12.

Primary: Number of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs)[1]

End point description:

AE: any adverse change from the subject's baseline (pre-treatment) condition, including any adverse experience, abnormal recording or clinical laboratory assessment value which occurs during the course of the study, whether it is considered related to the study drug or not. An adverse event includes any newly occurring event or previous condition that has increased in severity or frequency since the administration of study drug. SAE: medical event or condition, which falls into any of the following categories, regardless of its relationship to the study drug: death, life threatening adverse experience, in-patient hospitalization/prolongation of hospitalization, persistent/significant disability or incapacity, congenital anomaly/birth defect, important medical event. "Study drug" includes all investigational agents administered during the course of the study. Safety set included all subjects who received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

Baseline up to Week 52

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistics was planned for this endpoint.

End point values	Cohort 1 (13-17 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 2 (7-12 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 3 (3-6 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	19	10	
Units: subjects				
Subjects with SAEs	0	0	1	
Subjects with AEs	13	18	10	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Sustained Viral Response 12 Weeks After Last Planned Dose of Study Drug (SVR12)

End point title	Percentage of Subjects With Sustained Viral Response 12 Weeks After Last Planned Dose of Study Drug (SVR12)

End point description:

SVR12 was defined as an undetectable Hepatitis C Virus (HCV) Ribonucleic Acid (RNA) Levels (less than [<] lower limit of quantification) at 12 weeks after last planned dose of study drug. The plasma HCV RNA level was measured using Roche COBAS TaqMan HCV/High Pure System (HPS) RNA assay version 2.0. The lower limit of quantification was 25 international units per milliliter (IU/mL). Full analysis set (FAS) included all enrolled subjects who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

12 weeks after last planned dose of study drug (up to Week 60)

End point values	Cohort 1 (13-17 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 2 (7-12 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 3 (3-6 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	19	10	
Units: percentage of subjects				
number (not applicable)	69.2	89.5	40	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Sustained Viral Response 24 Weeks After Last Planned Dose of Study Drug (SVR24)

End point title	Percentage of Subjects With Sustained Viral Response 24 Weeks After Last Planned Dose of Study Drug (SVR24)

End point description:

SVR24 was defined as an undetectable HCV RNA Levels (< lower limit of quantification) at 24 weeks after last planned dose of study drug. The plasma HCV RNA level was measured using Roche COBAS TaqMan HCV/HPS RNA assay version 2.0. The lower limit of quantification was 25 IU/mL. SVR24 was not analyzed because study was terminated early and follow-up was conducted only up to 12 weeks after planned end of treatment (EOT).

End point type	Secondary

End point timeframe:

24 weeks after last planned dose of study drug (up to Week 72)

End point values	Cohort 1 (13-17 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 2 (7-12 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 3 (3-6 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[2]	0[3]	0[4]	
Units: percentage of subjects				
number (not applicable)				

Notes:

[2] - Not analysed as study terminated early and follow-up conducted only up to 12 weeks after EOT.

[3] - Not analysed as study terminated early and follow-up conducted only up to 12 weeks after EOT.

[4] - Not analysed as study terminated early and follow-up conducted only up to 12 weeks after EOT.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Rapid Virologic Response (RVR)

End point title	Percentage of Subjects With Rapid Virologic Response (RVR)

End point description:

The plasma HCV RNA level was measured using Roche COBAS TaqMan HCV/HPS RNA assay version 2.0. The lower limit of quantification was 25
IU/mL. RVR was defined as an undetectable HCV RNA (<lower limit of quantification) 4 weeks after the start of study treatment. FAS included all enrolled subjects who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Week 4

End point values	Cohort 1 (13-17 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 2 (7-12 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 3 (3-6 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	19	10	
Units: percentage of subjects				

number (not applicable)	69.2	73.7	70	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Extended Rapid Virologic Response (eRVR)

End point title	Percentage of Subjects With Extended Rapid Virologic Response (eRVR)

End point description:

The plasma HCV RNA level was measured using Roche COBAS TaqMan HCV/HPS RNA assay version 2.0. The lower limit of quantification was 25
IU/mL. eRVR was defined as an undetectable HCV RNA (<lower limit of quantification) at both 4 weeks and 12 weeks after the start of study
treatment. FAS included all enrolled subjects who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Week 4 and Week 12

End point values	Cohort 1 (13-17 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 2 (7-12 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 3 (3-6 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	19	10	
Units: percentage of subjects				
number (not applicable)	61.5	73.7	60	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Undetectable HCV RNA at Week 12

End point title	Percentage of Subjects With Undetectable HCV RNA at Week 12

End point description:

The plasma HCV RNA level was measured using Roche COBAS TaqMan HCV/HPS RNA assay version 2.0. The lower limit of quantification was 25
IU/mL. FAS included all enrolled subjects who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Week 12

End point values	Cohort 1 (13-17 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 2 (7-12 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 3 (3-6 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	19	10	
Units: percentage of subjects				
number (not applicable)	69.2	89.5	70	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With On-treatment Virologic Failure

End point title	Percentage of Subjects With On-treatment Virologic Failure

End point description:

On treatment virologic failure was defined as meeting any futility rule or completing assigned treatment duration and having detectable HCV RNA at EOT. The plasma HCV RNA level was measured using Roche COBAS TaqMan HCV/HPS RNA assay Version 2.0. The lower limit of quantification was 25 IU/mL. Futility rules: 1) HCV RNA >1000 IU/mL at Week 4; 2) HCV RNA >1000 IU/mL at Week 12; 3) Detectable HCV RNA after Week 12 to end of treatment. FAS included all enrolled subjects who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline up to Week 48

End point values	Cohort 1 (13-17 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 2 (7-12 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 3 (3-6 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	19	10	
Units: percentage of subjects				
number (not applicable)	15.4	5.3	30	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Virologic Relapse

End point title	Percentage of Subjects With Virologic Relapse

End point description:

The plasma HCV RNA level was measured using Roche COBAS TaqMan HCV/HPS RNA assay Version 2.0. The lower limit of quantification was 25 IU/mL. Viral relapse was defined as having detectable HCV at follow-up in subjects who had HCV RNA less than (<) lower limit of quantification (LLOQ) at planned EOT. FAS included all enrolled subjects who received at least 1 dose of study drug. Here 'Number of Subjects Analysed' signifies those subjects who completed the assigned treatment period and had undetectable HCV RNA at EOT.

End point type	Secondary

End point timeframe:

12 weeks after planned EOT (up to Week 60)

End point values	Cohort 1 (13-17 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 2 (7-12 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 3 (3-6 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	17	7	
Units: percentage of subjects				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Telaprevir Resistant HCV Variant at Non-Structural Viral Protein 3-4A (NS3-4A) Region

End point title	Number of Subjects With Telaprevir Resistant HCV Variant at Non-Structural Viral Protein 3-4A (NS3-4A) Region

End point description:

Sequence analysis of the HCV NS3-4A region was performed to monitor telaprevir-resistant variants. HCV RNA was isolated from the plasma, amplified by reverse transcription-polymerase chain reaction (RT-PCR), and sequenced (sequencing assay limit of detection HCV RNA >=1000 IU/mL). Results of this outcome measure were to be reported for overall subjects instead of by age. FAS. Here 'Number of Subjects Analysed' signifies those subjects who were evaluable for this outcome.

End point type	Secondary

End point timeframe:

Baseline, On treatment (up to Week 48)

End point values	Overall Subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	41[5]			
Units: subjects				
Baseline (n = 41)	2			
On treatment (n = 6)	6			

Notes:

[5] - 'n' signifies those subjects who were evaluable at the specified time points.

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Plasma Concentration (Cmax) of Telaprevir

End point title	Maximum Plasma Concentration (Cmax) of Telaprevir

End point description:

Cmax was measured for telaprevir only. Pharmacokinetic (PK) population included all subjects who received at least a single dose of telaprevir, whether the subject completed all treatments or not. Here 'Number of Subjects Analysed' signifies those subjects who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Cohort 1: Pre-dose and 0.5, 1.0, 2.0, 3.0, 4.0, 5.0, 6.0, and 8.0 hours post-dose on Day 7, Cohort 2: Pre-dose and 0.5, 2.0, 4.0, 5.0, 6.0, and 8.0 hours post-dose on Day 7, Cohort 3: Pre-dose and 1.5, 4.0, and 8.0 hours post-dose on Day 7

End point values	Cohort 1 (13-17 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 2 (7-12 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 3 (3-6 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	13	9	
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)	4310 (± 1160)	5050 (± 884)	4060 (± 1500)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Plasma Concentration (Tmax) of Telaprevir

End point title	Time to Reach Maximum Plasma Concentration (Tmax) of Telaprevir

End point description:

Tmax was measured for telaprevir only. PK population. Here 'Number of Subjects Analysed' signifies those subjects who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Cohort 1: Pre-dose and 0.5, 1.0, 2.0, 3.0, 4.0, 5.0, 6.0, and 8.0 hours post-dose on Day 7, Cohort 2: Pre-dose and 0.5, 2.0, 4.0, 5.0, 6.0, and 8.0 hours post-dose on Day 7, Cohort 3: Pre-dose and 1.5, 4.0, and 8.0 hours post-dose on Day 7

End point values	Cohort 1 (13-17 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 2 (7-12 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 3 (3-6 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	13	9	
Units: hours (h)				
median (full range (min-max))	4 (1.92 to 8)	4 (1.98 to 6.02)	4 (1.5 to 8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration Versus Time Curve (AUC) of Telaprevir

End point title	Area Under the Plasma Concentration Versus Time Curve (AUC) of Telaprevir

End point description:

AUC was measured for telaprevir only. AUC 0-t last was defined as the area under the concentration-time curve from the time of dosing to the last measurable concentration. AUC 0-12 hour (AUC 0-12h) was calculated by respecifying predose concentrations as 12 hour concentrations. AUC 0-24h was calculated as AUC 0-12h multiplied by 2. Dose adjusted AUC (AUC 0-24h_Adj) was calculated by multiplying AUC 0-24h by the dose adjustment factor to obtain projected exposures in subjects who were misdosed. Data were presented for AUC 0-t last, AUC 0-12h, AUC 0-24h, AUC 0-24h_Adj. PK population. Here 'Number of Subjects Analyzed' signifies those subjects who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Cohort 1: Pre-dose and 0.5, 1.0, 2.0, 3.0, 4.0, 5.0, 6.0, and 8.0 hours post-dose on Day 7, Cohort 2: Pre-dose and 0.5, 2.0, 4.0, 5.0, 6.0, and 8.0 hours post-dose on Day 7, Cohort 3: Pre-dose and 1.5, 4.0, and 8.0 hours post-dose on Day 7

End point values	Cohort 1 (13-17 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 2 (7-12 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 3 (3-6 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	13	9	
Units: hours*nanogram per milliliter (h*ng/mL)				
arithmetic mean (standard deviation)				
AUC 0-t last	39900 (± 11300)	43300 (± 9480)	35300 (± 12000)	
AUC 0-12h	39900 (± 11300)	44100 (± 9020)	35300 (± 12000)	

AUC 0-24h	79900 (± 22700)	88100 (± 18000)	70600 (± 24100)	
AUC 0-24h_Adj	95700 (± 29800)	88600 (± 19200)	76300 (± 22800)	

Statistical analyses

No statistical analyses for this end point

Secondary: Elimination Half-Life (T1/2) of Telaprevir

End point title	Elimination Half-Life (T1/2) of Telaprevir

End point description:

T1/2 was defined as the time required for the concentration or amount of drug in the body to be reduced by one-half. Half life was not calculated because the calculation required the slope of terminal elimination phase and the PK sampling was relatively sparse and did not yield a terminal elimination phase from which half-life can be accurately estimated.

End point type	Secondary

End point timeframe:

Cohort 1: Pre-dose and 0.5, 1.0, 2.0, 3.0, 4.0, 5.0, 6.0, and 8.0 hours post-dose on Day 7, Cohort 2: Pre-dose and 0.5, 2.0, 4.0, 5.0, 6.0, and 8.0 hours post-dose on Day 7, Cohort 3: Pre-dose and 1.5, 4.0, and 8.0 hours post-dose on Day 7

End point values	Cohort 1 (13-17 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 2 (7-12 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 3 (3-6 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[6]	0[7]	0[8]	
Units: hours (h)				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[6] - PK sampling sparse, did not yield terminal elimination phase from which half-life can be calculated.

[7] - PK sampling sparse, did not yield terminal elimination phase from which half-life can be calculated.

[8] - PK sampling sparse, did not yield terminal elimination phase from which half-life can be calculated.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to Week 52

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Cohort 1 (13-17 Years): Telaprevir + Peg-IFN-alfa-2b + RBV

Reporting group description:

Subjects aged 13 to 17 years received telaprevir twice daily for 12 weeks either as a film coated tablet (15 mg/kg of body weight) or as a chewable tablet (14 mg/kg of body weight) in combination with Peg-IFN-alfa-2b 60 mcg/m^2 subcutaneous injection weekly and RBV 200 mg capsules or 40 mg/mL solution orally twice daily with a maximum dose of 1200 mg per day. Peg-IFN-alfa-2b and RBV were administered for 24 weeks in subjects who achieved eRVR or for 48 weeks in subjects who did not achieve eRVR. eRVR was defined as undetectable HCV RNA levels at Week 4 and Week 12.

Reporting group title	Cohort 2 (7-12 Years): Telaprevir + Peg-IFN-alfa-2b + RBV

Reporting group description:

Subjects aged 7 to 12 years received telaprevir twice daily for 12 weeks as a chewable tablet (16 mg/kg of body weight) in combination with Peg-IFN-alfa-2b 60 mcg/m^2 subcutaneous injection weekly and RBV 200-mg capsules or 40 mg/mL solution orally twice daily with a maximum dose of 1200 mg per day. Peg-IFN-alfa-2b and RBV were administered for 24 weeks in subjects who achieved eRVR or for 48 weeks in subjects who did not achieve eRVR. eRVR was defined as undetectable HCV RNA levels at Week 4 and Week 12.

Reporting group title	Cohort 3 (3-6 Years): Telaprevir + Peg-IFN-alfa-2b + RBV

Reporting group description:

Subjects aged 3 to 6 years received telaprevir twice daily for 12 weeks as a chewable tablet (18 mg/kg of body weight) in combination with Peg-IFN-alfa-2b 60 mcg/m^2 subcutaneous injection weekly and RBV 200-mg capsules or 40 mg/mL solution orally twice daily with a maximum dose of 1200 mg per day. Peg-IFN-alfa-2b and RBV were administered for 24 weeks in subjects who achieved eRVR or for 48 weeks in subjects who did not achieve eRVR. eRVR was defined as undetectable HCV RNA levels at Week 4 and Week 12.

Serious adverse events	Cohort 1 (13-17 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 2 (7-12 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 3 (3-6 Years): Telaprevir + Peg-IFN-alfa-2b + RBV
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)	0 / 19 (0.00%)	1 / 10 (10.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 19 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Cohort 1 (13-17 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 2 (7-12 Years): Telaprevir + Peg-IFN-alfa-2b + RBV	Cohort 3 (3-6 Years): Telaprevir + Peg-IFN-alfa-2b + RBV
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 13 (100.00%)	18 / 19 (94.74%)	10 / 10 (100.00%)
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Pallor			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	7 / 13 (53.85%)	11 / 19 (57.89%)	8 / 10 (80.00%)
occurrences (all)	35	38	75
Fatigue			
subjects affected / exposed	7 / 13 (53.85%)	5 / 19 (26.32%)	3 / 10 (30.00%)
occurrences (all)	7	11	7
Pain			
subjects affected / exposed	2 / 13 (15.38%)	4 / 19 (21.05%)	5 / 10 (50.00%)
occurrences (all)	6	8	23
Injection site erythema			
subjects affected / exposed	3 / 13 (23.08%)	2 / 19 (10.53%)	3 / 10 (30.00%)
occurrences (all)	3	2	5
Influenza like illness			
subjects affected / exposed	1 / 13 (7.69%)	2 / 19 (10.53%)	1 / 10 (10.00%)
occurrences (all)	1	3	2
Chills			
subjects affected / exposed	2 / 13 (15.38%)	0 / 19 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	2
Discomfort			
subjects affected / exposed	1 / 13 (7.69%)	2 / 19 (10.53%)	0 / 10 (0.00%)
occurrences (all)	2	10	0
Injection site pruritus			

subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	1
Injection site rash			
subjects affected / exposed	1 / 13 (7.69%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Malaise			
subjects affected / exposed	2 / 13 (15.38%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	4	0	0
Non-cardiac chest pain			
subjects affected / exposed	2 / 13 (15.38%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	3	0	0
Product taste abnormal			
subjects affected / exposed	0 / 13 (0.00%)	2 / 19 (10.53%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Injection site bruising			
subjects affected / exposed	0 / 13 (0.00%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Injection site reaction			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Peripheral swelling			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Temperature intolerance			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Vessel puncture site pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	2 / 13 (15.38%)	0 / 19 (0.00%)	2 / 10 (20.00%)
occurrences (all)	2	0	6
Reproductive system and breast disorders			

Dysmenorrhoea			
subjects affected / exposed	1 / 13 (7.69%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	1	3	0
Amenorrhoea			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Oligomenorrhoea			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Pruritus genital			
subjects affected / exposed	0 / 13 (0.00%)	0 / 19 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 13 (0.00%)	2 / 19 (10.53%)	2 / 10 (20.00%)
occurrences (all)	0	3	5
Cough			
subjects affected / exposed	0 / 13 (0.00%)	2 / 19 (10.53%)	1 / 10 (10.00%)
occurrences (all)	0	3	1
Dyspnoea			
subjects affected / exposed	2 / 13 (15.38%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	3	1	0
Dyspnoea exertional			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 19 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Paranasal sinus hypersecretion			
subjects affected / exposed	0 / 13 (0.00%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Respiratory distress			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Rhinitis allergic			

subjects affected / exposed	0 / 13 (0.00%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 13 (15.38%)	1 / 19 (5.26%)	1 / 10 (10.00%)
occurrences (all)	2	2	1
Depression			
subjects affected / exposed	1 / 13 (7.69%)	2 / 19 (10.53%)	0 / 10 (0.00%)
occurrences (all)	1	2	0
Affect lability			
subjects affected / exposed	0 / 13 (0.00%)	0 / 19 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Mood altered			
subjects affected / exposed	0 / 13 (0.00%)	2 / 19 (10.53%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Mood swings			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Agitation			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Anxiety			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Flat affect			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Restlessness			
subjects affected / exposed	0 / 13 (0.00%)	0 / 19 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Sleep terror			
subjects affected / exposed	0 / 13 (0.00%)	0 / 19 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Investigations			
Blood bicarbonate decreased			

subjects affected / exposed	2 / 13 (15.38%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Blood triglycerides increased			
subjects affected / exposed	0 / 13 (0.00%)	2 / 19 (10.53%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Blood uric acid increased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 19 (5.26%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Weight decreased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	1
Alanine aminotransferase increased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Blood bilirubin increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Body temperature increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 19 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Haemoglobin decreased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 13 (15.38%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	2	1	0
Excoriation			

subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Limb injury			
subjects affected / exposed	0 / 13 (0.00%)	0 / 19 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Skin abrasion			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 13 (61.54%)	16 / 19 (84.21%)	6 / 10 (60.00%)
occurrences (all)	31	79	12
Dizziness			
subjects affected / exposed	5 / 13 (38.46%)	5 / 19 (26.32%)	0 / 10 (0.00%)
occurrences (all)	7	6	0
Lethargy			
subjects affected / exposed	0 / 13 (0.00%)	0 / 19 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Presyncope			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Somnolence			
subjects affected / exposed	0 / 13 (0.00%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 13 (30.77%)	5 / 19 (26.32%)	1 / 10 (10.00%)
occurrences (all)	6	5	1
Neutropenia			
subjects affected / exposed	4 / 13 (30.77%)	3 / 19 (15.79%)	2 / 10 (20.00%)
occurrences (all)	4	5	2
Leukopenia			

subjects affected / exposed	1 / 13 (7.69%)	4 / 19 (21.05%)	1 / 10 (10.00%)
occurrences (all)	1	5	1
Lymphadenopathy			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Thrombocytopenia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 19 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Eye disorders			
Eye irritation			
subjects affected / exposed	0 / 13 (0.00%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Eye pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 19 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Eye pruritus			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Mydriasis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Vision blurred			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	8 / 13 (61.54%)	12 / 19 (63.16%)	6 / 10 (60.00%)
occurrences (all)	13	23	12
Nausea			
subjects affected / exposed	7 / 13 (53.85%)	5 / 19 (26.32%)	5 / 10 (50.00%)
occurrences (all)	9	9	14
Anal pruritus			

subjects affected / exposed	4 / 13 (30.77%)	4 / 19 (21.05%)	3 / 10 (30.00%)
occurrences (all)	6	5	3
Abdominal pain			
subjects affected / exposed	5 / 13 (38.46%)	3 / 19 (15.79%)	1 / 10 (10.00%)
occurrences (all)	5	9	1
Abdominal pain upper			
subjects affected / exposed	2 / 13 (15.38%)	5 / 19 (26.32%)	0 / 10 (0.00%)
occurrences (all)	2	6	0
Diarrhoea			
subjects affected / exposed	2 / 13 (15.38%)	3 / 19 (15.79%)	0 / 10 (0.00%)
occurrences (all)	2	6	0
Abdominal distension			
subjects affected / exposed	2 / 13 (15.38%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Abdominal discomfort			
subjects affected / exposed	0 / 13 (0.00%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Anal fissure			
subjects affected / exposed	0 / 13 (0.00%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Anorectal discomfort			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Aphthous stomatitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Cheilitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	0 / 13 (0.00%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Diarrhoea haemorrhagic			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Dry mouth			

subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Gingival pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Lip ulceration			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Mouth ulceration			
subjects affected / exposed	0 / 13 (0.00%)	0 / 19 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Oral disorder			
subjects affected / exposed	0 / 13 (0.00%)	0 / 19 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Oral pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Tooth impacted			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	0 / 13 (0.00%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	3 / 13 (23.08%)	5 / 19 (26.32%)	3 / 10 (30.00%)
occurrences (all)	3	10	3
Rash			
subjects affected / exposed	4 / 13 (30.77%)	2 / 19 (10.53%)	3 / 10 (30.00%)
occurrences (all)	6	2	6
Alopecia			
subjects affected / exposed	7 / 13 (53.85%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	7	1	0

Pruritus generalised			
subjects affected / exposed	1 / 13 (7.69%)	3 / 19 (15.79%)	0 / 10 (0.00%)
occurrences (all)	1	8	0
Dry skin			
subjects affected / exposed	0 / 13 (0.00%)	0 / 19 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Erythema			
subjects affected / exposed	1 / 13 (7.69%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	1	4	0
Skin lesion			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Cold sweat			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Eczema			
subjects affected / exposed	0 / 13 (0.00%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Rash macular			
subjects affected / exposed	0 / 13 (0.00%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Rash papular			
subjects affected / exposed	0 / 13 (0.00%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Skin irritation			
subjects affected / exposed	0 / 13 (0.00%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 13 (15.38%)	2 / 19 (10.53%)	0 / 10 (0.00%)
occurrences (all)	2	3	0
Pain in extremity			
subjects affected / exposed	2 / 13 (15.38%)	2 / 19 (10.53%)	0 / 10 (0.00%)
occurrences (all)	6	2	0
Myalgia			

subjects affected / exposed	1 / 13 (7.69%)	2 / 19 (10.53%)	0 / 10 (0.00%)
occurrences (all)	1	2	0
Arthralgia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Neck pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 19 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Infections and infestations			
Oral herpes			
subjects affected / exposed	1 / 13 (7.69%)	1 / 19 (5.26%)	1 / 10 (10.00%)
occurrences (all)	1	1	1
Bronchitis			
subjects affected / exposed	1 / 13 (7.69%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Pharyngitis streptococcal			
subjects affected / exposed	0 / 13 (0.00%)	0 / 19 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Sinusitis			
subjects affected / exposed	2 / 13 (15.38%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	3	0	0
Urinary tract infection			
subjects affected / exposed	2 / 13 (15.38%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	2 / 13 (15.38%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Conjunctivitis bacterial			
subjects affected / exposed	0 / 13 (0.00%)	0 / 19 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Ear infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 19 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 19 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1

Gastroenteritis viral			
subjects affected / exposed	0 / 13 (0.00%)	0 / 19 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Hordeolum			
subjects affected / exposed	0 / 13 (0.00%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Parvovirus infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 19 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Rash pustular			
subjects affected / exposed	0 / 13 (0.00%)	0 / 19 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Skin infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Tinea infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Tonsillitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 13 (23.08%)	5 / 19 (26.32%)	3 / 10 (30.00%)
occurrences (all)	3	6	3
Abnormal loss of weight			

subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Dehydration			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 19 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Hyperinsulinaemia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 19 (5.26%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Hypocalcaemia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 19 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 March 2012	1) Clarification that subjects in Part A were to be without cirrhosis. 2) Number of subjects was changed from approximately 120 to at least 120, and the minimum number of subjects with prior peginterferon/RBV treatment was increased from 15 to 25. The number of subjects per age group in Part A was clarified to be at least 10 in the older age groups and at least 6 in the youngest age group. 3) Language was changed to specify that at least 30% of all subjects would be from each gender; that half of all subjects would be from the EU, US, or Canada; and that efforts would be made to include subjects from all races. 4) Clarification that the follow-up period would be 5 years from the last dose of study drug (instead of 5 years from the first dose of study drug). 5) Descriptions of informed consent and assent were simplified in anticipation of differences in local (country-specific) rules/regulations. Specifically, statements that assent would be for children older than 12 years were removed. 6) Information on study drug dosing was updated, including addition of language to state that dosing for telaprevir would be based on the subject's baseline weight, and that the dose for Peg-IFN and RBV would be adjusted using the subject's current weight at Week 24, if necessary. 7) Ferritin and serology tests for hepatitis C virus and hepatitis A virus were added to the list of assessments to be performed at screening and positive result for anti-hepatitis A virus immunoglobulin M antibody was made an exclusion. 8) Information on detection of liver disease at baseline was updated. It was clarified that results from recent (within 24 months of screening) liver biopsies, if available, would be collected. 9) An exclusion criterion was added for any disease of iron overload, including hemochromatosis, and diseases requiring repeat transfusions. 10) Clarification that a urine home pregnancy test kit would be provided when there were no scheduled study visits.
21 June 2012	1) Body weight less than 15 kg was made an exclusion criterion for both Part A and Part B of the study. 2) Exclusions for screening laboratory values were modified to be consistent with regulatory requirements. Exclusions related to thyroid dysfunction were modified. A new exclusion criterion was added for subjects who were pregnant, breastfeeding, or planning to get pregnant during study drug administration or within 6 months after the last dose of RBV. 3) "History of intercurrent illness (e.g., upper respiratory illness with fever) within 5 days prior to the first dose of study drug" was made an exclusion criterion. 4) The exclusion criterion with respect to participation in other studies of investigational drugs was significantly modified, including types of studies, time of previous blood draws, and use of a protease inhibitor. 5) Clarification that subjects in Part B could be with or without cirrhosis. 6) The exclusion criterion on previous treatment experience was clarified to state that subjects in Part A could not have been previously treated with any approved or experimental treatment for hepatitis C. 7) The PK blood sample at 12 hours postdose was deleted. 8) The section on contraception was updated for consistency with regulatory guidance and for clarity. 9) Clarification that telaprevir and RBV were to be taken with food within 30 minutes after eating a meal or snack that was not low fat. 10) The recommendation that the chewable tablets could be crushed and taken with whole milk was removed due to new food testing results. 11) Clarification that investigators were to evaluate subjects' HCV RNA results by Week 24 and inform subject parents/guardians of their total treatment duration. 12) Clarification of scheduling of follow-up visits and assessments to be performed at these visits and futility rules. 14) Canada was removed in the description of the study population because no sites were planned for this country.

29 August 2012	1) The allowance for an overnight visit the night before Day 7 was removed. 2) A mandatory second visit during the screening period was added for laboratory draws (HCV genotype/subtype, HCV serology, human immunodeficiency virus serology, hepatitis A virus serology, hepatitis B virus serology and DNA and antinuclear antibody) for children in the 3- to 6-year-old and 7- to 12-year-old age groups. This was implemented to ensure that the maximum allowable blood volume drawn was not exceeded. 3) References to the use of a breath alcohol test were removed from the document and replaced with a urine alcohol test. The drug and alcohol tests planned for the treatment period were deleted. 4) The time points for ophthalmologic examinations planned for the treatment/follow-up periods were changed to align with the recommendations in the package insert for Peg-IFN. 5) Exclusion criteria for low hemoglobin and for ophthalmologic disorders were clarified and made more specific.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Study was terminated early because it was determined that telaprevir/Peg-IFN/RBV regimen did not present a meaningful therapeutic treatment over existing interferon-free regimens and was unlikely to be used for subjects aged 3 to 17 years.

Notes: