Clinical trial results:
Multicenter, Open-Label, Early Access Program of Telaprevir in Combination With Peginterferon Alfa and Ribavirin in Genotype 1 Chronic Hepatitis C Subjects With Severe Fibrosis and Compensated Cirrhosis

Summary

EudraCT number	2010-023669-23
Trial protocol	AT IT CZ GR ES HU SK
Global end of trial date	30 May 2014

Results information

Result version number	v2 (current)
This version publication date	23 June 2016
First version publication date	02 August 2015
Version creation reason	• Correction of full data set Review of data

Trial information

Trial identification

Sponsor protocol code	VX-950HEP3002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01508286
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen-Cilag International NV
Sponsor organisation address	Antwerpseweg 15-17, Beerse, Belgium, B-2340
Public contact	Janssen-Cilag International NV - Clinical Registry Group, Janssen Biologics BV, ClinicalTrialsEU@its.jnj.com
Scientific contact	Janssen-Cilag International NV - Clinical Registry Group, Janssen Biologics BV, ClinicalTrialsEU@its.jnj.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 May 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 May 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this early access program was to provide telaprevir for participants with genotype 1 chronic hepatitis C with severe fibrosis or compensated cirrhosis who resided in countries in which telaprevir was not commercially available at the time of protocol writing and who were not eligible for enrollment into an ongoing clinical study of telaprevir, and to collect additional safety and tolerability data on telaprevir treatment in combination with pegylated interferon alpha (Peg-IFN-alfa) and ribavirin (RBV).

Protection of trial subjects:

Assessment of safety and tolerability was based on reported adverse events (AEs), clinical laboratory tests, vital sign measurements, electrocardiogram (ECG) monitoring, and physical examinations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 May 2011
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	Australia: 60
Country: Number of subjects enrolled	Austria: 23
Country: Number of subjects enrolled	Belgium: 53
Country: Number of subjects enrolled	Brazil: 97
Country: Number of subjects enrolled	Switzerland: 17
Country: Number of subjects enrolled	Czech Republic: 45
Country: Number of subjects enrolled	Germany: 95
Country: Number of subjects enrolled	Greece: 29
Country: Number of subjects enrolled	Spain: 160
Country: Number of subjects enrolled	Hungary: 134
Country: Number of subjects enrolled	Italy: 568
Country: Number of subjects enrolled	Luxembourg: 4
Country: Number of subjects enrolled	New Zealand: 21
Country: Number of subjects enrolled	Romania: 218
Country: Number of subjects enrolled	Russian Federation: 185
Country: Number of subjects enrolled	Serbia: 63
Worldwide total number of subjects	1772
EEA total number of subjects	1329

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	1585
From 65 to 84 years	187
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 2034 participants were screened for this early access program. Of these, 1772 participants were treated with telaprevir. 1587 participants completed the early access program.

Period 1

Period 1 title	Overall (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Telaprevir + Pegylated Interferon/Ribavirin

Arm description:

Participants received Telaprevir 750 milligram (mg) (2*375 mg) tablet orally every 8 hours for the first 12 weeks of the early access program in combination with Pegylated Interferon/Ribavirin followed by 12 or 36 weeks of treatment with Pegylated Interferon/Ribavirin alone.

Arm type	Experimental
Investigational medicinal product name	Telaprevir
Investigational medicinal product code	VX-950
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants were received Telaprevir 750 (2*375) milligram (mg) tablet orally every 8 hours for first 12 weeks of the early access program in combination with Pegylated Interferon/Ribavirin.

Number of subjects in period 1	Telaprevir + Pegylated Interferon/Ribavirin
Started	1772
Completed	1587
Not completed	185
Adverse event, serious fatal	9
Consent withdrawn by subject	75
Adverse event, non-fatal	2
Other	7
Participant entered another investigational trial	2
Lost to follow-up	90

Baseline characteristics

Reporting groups	
Reporting group title	Telaprevir + Pegylated Interferon/Ribavirin
Reporting group description:	
Participants received Telaprevir 750 milligram (mg) (2*375 mg) tablet orally every 8 hours for the first 12 weeks of the early access program in combination with Pegylated Interferon/Ribavirin followed by 12 or 36 weeks of treatment with Pegylated Interferon/Ribavirin alone.	

Reporting group values	Telaprevir + Pegylated Interferon/Ribavirin	Total	
Number of subjects	1772	1772	
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	1585	1585	
From 65 to 84 years	187	187	
85 years and over	0	0	
Title for AgeContinuous Units: years			
arithmetic mean	53		
standard deviation	± 9.49	-	
Title for Gender Units: subjects			
Female	651	651	
Male	1121	1121	

End points

End points reporting groups

Reporting group title	Telaprevir + Pegylated Interferon/Ribavirin

Reporting group description:

Participants received Telaprevir 750 milligram (mg) (2*375 mg) tablet orally every 8 hours for the first 12 weeks of the early access program in combination with Pegylated Interferon/Ribavirin followed by 12 or 36 weeks of treatment with Pegylated Interferon/Ribavirin alone.

Subject analysis set title	Treatment naive
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants who had never received hepatitis C virus (HCV) drugs.

Subject analysis set title	Prior relapser
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants with confirmed detectable hepatitis C virus (HCV) ribonucleic acid (RNA) during the follow-up period after previous HCV RNA 'less than (<) lower limit of quantification (LLOQ), target not detected' at the end of treatment.

Subject analysis set title	Prior null responder
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants who had a < 2-log10 decrease in HCV RNA level at Week 12 compared to baseline HCV RNA level during prior treatment.

Subject analysis set title	Prior partial responder
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants who had a greater than or equal to (>=) 2-log10 decrease in HCV RNA level at Week 12 compared to baseline HCV RNA level, but never had HCV RNA '<LLOQ, target not detected' during prior treatment.

Subject analysis set title	Prior non-responder
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants who never had HCV RNA '<LLOQ, target not detected' during prior treatment. This includes prior null responder and prior partial responder.

Subject analysis set title	Viral breakthroughs
Subject analysis set type	Intention-to-treat

Subject analysis set description:

A confirmed increase greater than (>) 1 log10 in HCV RNA level from the lowest level reached during the considered treatment phase up to the considered time point, if the lowest level reached was >LLOQ, or a confirmed value of HCV RNA >100 International units per milliliter (IU/mL) in participants whose HCV RNA had previously become <LLOQ ('target detected' or 'target not detected') during the considered treatment phase.

Primary: Percentage of Participants Achieving Sustained Virologic Response (SVR) 24actual (Snapshot, less than [<] lower limit of quantification [LLOQ]) 24 Weeks After the Last Actual Dose of Hepatitis C Virus (HCV) Drug

End point title	Percentage of Participants Achieving Sustained Virologic Response (SVR) 24actual (Snapshot, less than [<] lower limit of quantification [LLOQ]) 24 Weeks After the Last Actual Dose of Hepatitis C Virus (HCV) Drug[1]

End point description:

The SVR24actual (Snapshot, <LLOQ), defined as achieving HCV RNA <LLOQ at the last nonmissing measurement in the Week 24 Follow-up visit window (that is, date from last intake of HCV drug [telaprevir, Peg-IFN-alfa, or RBV] +71 days until date of last contact).

End point type	Primary

End point timeframe:

Week 72

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: Descriptive statistics were done, no inferential statistical analyses were performed

End point values	Treatment naive	Prior relapser	Prior null responder	Prior partial responder
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	355	586	495	234
Units: Percentage				
number (not applicable)	73.8	78.2	44	60.3

End point values	Prior non-responder			
Subject group type	Subject analysis set			
Number of subjects analysed	830			
Units: Percentage				
number (not applicable)	50.5			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Achieving Sustained Virologic Response (SVR) 24actual (Snapshot, 'less than [<] lower limit of quantification [LLOQ], target not detected') 24 Weeks After the Last Actual Dose of Hepatitis C Virus (HCV) Drug

End point title	Percentage of Participants Achieving Sustained Virologic Response (SVR) 24actual (Snapshot, 'less than [<] lower limit of quantification [LLOQ], target not detected') 24 Weeks After the Last Actual Dose of Hepatitis C Virus (HCV) Drug[2]

End point description:

The SVR24actual (Snapshot, '<LLOQ, target not detected'), defined as achieving HCV RNA '<LLOQ, target not detected' at the last nonmissing measurement in the Week 24 Follow-up visit window.

End point type	Primary

End point timeframe:

Week 72

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: Descriptive statistics were done, no inferential statistical analyses were performed

End point values	Treatment naive	Prior relapser	Prior null responder	Prior partial responder
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	355	586	495	234
Units: Percentage				
number (not applicable)	73.5	77.6	43.8	60.3

End point values	Prior non-responder			
Subject group type	Subject analysis set			
Number of subjects analysed	830			
Units: Percentage				
number (not applicable)	50.2			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Achieving Sustained Virologic Response (SVR) 24actual (Classic) 24 Weeks After the Last Actual Dose of Hepatitis C Virus (HCV) Drug

End point title	Percentage of Participants Achieving Sustained Virologic Response (SVR) 24actual (Classic) 24 Weeks After the Last Actual Dose of Hepatitis C Virus (HCV) Drug[3]

End point description:

The SVR24actual (Classic), defined as having HCV RNA '<LLOQ, target not detected' at End of Treament, and having at least one nonmissing HCV RNA measurement in the Week 24 Follow-up visit window, and not having relapsed, and having completed treatment (all HCV drugs) or having permanently discontinued at least one of the HCV drugs but for a reason other than virologic failure.

End point type	Primary

End point timeframe:

Week 72

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics were done, no inferential statistical analyses were performed

End point values	Treatment naive	Prior relapser	Prior null responder	Prior partial responder
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	317	538	427	214
Units: Percentage				
number (not applicable)	79.5	83.8	50.1	64.5

End point values	Prior non-responder			
Subject group type	Subject analysis set			
Number of subjects analysed	733			
Units: Percentage				
number (not applicable)	55.8			

Statistical analyses

No statistical analyses for this end point

Primary: Log10 Hepatitis C Virus (HCV) Ribonucleic Acid (RNA) Values at Each Time Point During Treatment

End point title	Log10 Hepatitis C Virus (HCV) Ribonucleic Acid (RNA) Values at Each Time Point During Treatment[4]

End point description:

Change from baseline in log10 of Plasma Hepatitis C Virus (HCV) ribonucleic acid (RNA) levels were measured using HCV test (lower limit of quantification 25 international units/milliliter [IU/mL]). The assay used real-time reverse transcription - polymerase chain reaction (RT-PCR) methodology. HCV RNA samples were taken pre-dose of Pegylated-interferon (Peg-IFN) administration.

End point type	Primary

End point timeframe:

Baseline and Week 4

Notes:

[4] - 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: Descriptive statistics were done, no inferential statistical analyses were performed

End point values	Treatment naive	Prior relapser	Prior non-responder	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	355	586	830	
Units: International unit per milliliter(IU/ml)				
arithmetic mean (standard deviation)				
Baseline (n= 355, 586, 830)	6 (± 0.76)	6.1 (± 0.72)	6.2 (± 0.66)	
Change at Week 4 (n= 329, 586, 830)	-5.04 (± 0.892)	-5.1 (± 0.812)	-4.96 (± 1.018)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Achieving Rapid Virologic Response (RVR) at Week 4

End point title	Percentage of Participants Achieving Rapid Virologic Response (RVR) at Week 4[5]

End point description:

Percentage of participants who had a Rapid Virologic Response (RVR) (that is, those with undetectable hepatitis C virus [HCV] ribonucleic acid [RNA] values of less than 25 international units/milliliter [IU/mL], target not detected at Weeks 4 of treatment) were evaluated.

End point type	Primary

End point timeframe:

Week 4

Notes:

[5] - 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: Descriptive statistics were done, no inferential statistical analyses were performed

End point values	Treatment naive	Prior relapser	Prior non-responder	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	355	586	830	
Units: Percentage				
number (not applicable)	63.9	69.6	50.7	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Achieving Extended Rapid Virologic Response (eRVR) at Weeks 4 and 12

End point title	Percentage of Participants Achieving Extended Rapid Virologic Response (eRVR) at Weeks 4 and 12[6]

End point description:

Percentage of participants who had a Extended Rapid Virologic Response (eRVR) (that is, those with undetectable hepatitis C virus [HCV] ribonucleic acid [RNA] values of less than 25 international units/milliliter [IU/mL], target not detected at Weeks 4 and 12 of treatment) were evaluated.

End point type	Primary

End point timeframe:

Week 4 and 12

Notes:

[6] - 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: Descriptive statistics were done, no inferential statistical analyses were performed

End point values	Treatment naive	Prior relapser	Prior non-responder	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	355	586	830	
Units: Percentage				
number (not applicable)	59.2	65.4	45.8	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Having Virologic Response at End of Treatment (Week 24 or 48)

End point title	Percentage of Participants Having Virologic Response at End of Treatment (Week 24 or 48)[7]

End point description:

Virologic response was either defined as having undetectable Hepatitis C Virus (HCV) ribonucleic acid (RNA) (that is, no HCV RNA was detected in the participants' plasma samples) or less than 25 international units/milliliter (IU/mL) HCV RNA (that is, the participants' plasma samples contained traces of HCV RNA at a concentration below the limit of quantification of the viral load assay or no HCV RNA was detected in the samples).

End point type	Primary

End point timeframe:

Week 24 or 48

Notes:

[7] - 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: Descriptive statistics were done, no inferential statistical analyses were performed

End point values	Treatment naive	Prior relapser	Prior null responder	Prior partial responder
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	355	586	495	234
Units: Percentage				
number (not applicable)				
Viral Response ('<LLOQ, target not detected')	79.4	84.8	54.7	75.2
Viral Response (<LLOQ)	81.7	85.7	58.2	78.2

End point values	Prior non-responder			
Subject group type	Subject analysis set			
Number of subjects analysed	830			
Units: Percentage				
number (not applicable)				
Viral Response ('<LLOQ, target not detected')	62.3			
Viral Response (<LLOQ)	65.4			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Viral Breakthrough

End point title	Percentage of Participants With Viral Breakthrough[8]

End point description:

A confirmed increase >1 log10 in HCV RNA level from the lowest level reached during the considered treatment phase up to the considered time point, if the lowest level reached was >LLOQ, or a confirmed value of HCV RNA >100 IU/mL in participants whose HCV RNA had previously become <LLOQ (detectable or 'target not detected') during the considered treatment phase.

End point type	Primary

End point timeframe:

Up to Week 48

Notes:

[8] - 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: Descriptive statistics were done, no inferential statistical analyses were performed

End point values	Treatment naive	Prior relapser	Prior null responder	Prior partial responder
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	355	586	495	234
Units: Percentage				
number (not applicable)				
Week 4	0	0.2	0.2	0
Week 8	0	0	2.6	0.4
Week 12	2	1.2	7.5	2.6
Week 24	5.9	4.1	18.8	7.7
Week 48	7.9	4.8	24.6	11.5

End point values	Prior non-responder			
Subject group type	Subject analysis set			
Number of subjects analysed	830			
Units: Percentage				
number (not applicable)				
Week 4	0.1			
Week 8	1.8			
Week 12	5.5			
Week 24	14.6			
Week 48	19.3			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants who Relapsed

End point title	Percentage of Participants who Relapsed[9]

End point description:

Relapse (<LLOQ), defined as having HCV RNA <LLOQ at EOT and HCV RNA detectable during the follow-up phase, and not achieving SVR24actual (Snapshot, <LLOQ); or Relapse (‘<LLOQ, target not detected’), defined similarly with the ‘<LLOQ, target not detected’ threshold.

End point type	Primary

End point timeframe:

Week 72

Notes:

[9] - 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: Descriptive statistics were done, no inferential statistical analyses were performed

End point values	Treatment naive	Prior relapser	Prior null responder	Prior partial responder
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	355	586	495	234
Units: Percentage				
number (not applicable)				
25 -< 2000 IU/mL (n = 290, 502, 288, 183, 543)	0.7	0.8	1	1.1
>= 2000 IU/mL (n = 290, 502, 288, 183, 543)	8.3	7.6	21.5	20.2
Qualitative Detectable(n =290, 502, 288, 183, 543)	0.7	0.4	1.4	0.5

End point values	Prior non-responder			
Subject group type	Subject analysis set			
Number of subjects analysed	830			
Units: Percentage				
number (not applicable)				
25 -< 2000 IU/mL (n = 290, 502, 288, 183, 543)	1.1			
>= 2000 IU/mL (n = 290, 502, 288, 183, 543)	20.3			
Qualitative Detectable(n =290, 502, 288, 183, 543)	1.1			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants who met a Virologic Stopping Rule

End point title	Percentage of Participants who met a Virologic Stopping Rule[10]

End point description:

Stopping rules based on virologic response at Weeks 4 and 12 were to be applied to ensure that telaprevir or Peg-IFN-alfa/RBV treatments were stopped if a participant had viral breakthrough or failure.

End point type	Primary

End point timeframe:

Week 4 and 12

Notes:

[10] - 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: Descriptive statistics were done, no inferential statistical analyses were performed

End point values	Treatment naive	Prior relapser	Prior null responder	Prior partial responder
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	355	586	495	234
Units: Participants				
number (not applicable)				
Telaprevir stopping rule – Week 4	2	0.5	5.5	1.3
RBV/Peg-IFN stopping rule – Week 12	2.3	0.7	5.9	1.3

End point values	Prior non-responder			
Subject group type	Subject analysis set			
Number of subjects analysed	830			
Units: Participants				
number (not applicable)				
Telaprevir stopping rule – Week 4	4.1			
RBV/Peg-IFN stopping rule – Week 12	4			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to Week 72	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	11.0
Reporting groups	
Reporting group title	Telaprevir + Pegylated Interferon/Ribavirin
Reporting group description:	
Participants received Telaprevir 750 milligram (mg) (2*375 mg) tablet orally every 8 hours for the first 12 weeks of the early access program in combination with Pegylated Interferon/Ribavirin.	

Serious adverse events	Telaprevir + Pegylated Interferon/Ribavirin		
Total subjects affected by serious adverse events			
subjects affected / exposed	147 / 1772 (8.30%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events			
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Face Oedema			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Asthenia			
subjects affected / exposed	3 / 1772 (0.17%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Influenza Like Illness			

subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Fatigue			
subjects affected / exposed	3 / 1772 (0.17%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Malaise			
subjects affected / exposed	2 / 1772 (0.11%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Multi-Organ Failure			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Non-Cardiac Chest Pain			
subjects affected / exposed	2 / 1772 (0.11%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	9 / 1772 (0.51%)		
occurrences causally related to treatment / all	4 / 9		
deaths causally related to treatment / all	0 / 0		
Pain			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Testicular Mass			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			

Dyspnoea				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cough				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Interstitial Lung Disease				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Confusional State				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Alanine Aminotransferase Increased				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Haemoglobin Decreased				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Transaminases Increased				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Weight Decreased				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal Injury			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial Fibrillation			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Coronary Artery Disease			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac Failure			
subjects affected / exposed	2 / 1772 (0.11%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Palpitations			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Coma			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Dizziness			

subjects affected / exposed	2 / 1772 (0.11%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Hepatic Encephalopathy				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Encephalopathy				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
alternative assessment type: Systematic				
subjects affected / exposed	73 / 1772 (4.12%)			
occurrences causally related to treatment / all	73 / 73			
deaths causally related to treatment / all	1 / 1			
Bone Marrow Failure				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Leukopenia				
subjects affected / exposed	3 / 1772 (0.17%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Lymphopenia				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Neutropenia				
subjects affected / exposed	5 / 1772 (0.28%)			
occurrences causally related to treatment / all	3 / 6			
deaths causally related to treatment / all	0 / 0			

Neutrophilia				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	4 / 1772 (0.23%)			
occurrences causally related to treatment / all	2 / 4			
deaths causally related to treatment / all	0 / 0			
Pancytopenia				
subjects affected / exposed	2 / 1772 (0.11%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Retinal Disorder				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Retinal Haemorrhage				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal Pain				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Anal Fissure				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Ascites				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Erosive Duodenitis				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastritis				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal Haemorrhage				
subjects affected / exposed	2 / 1772 (0.11%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Haemorrhoidal Haemorrhage				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal Obstruction				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	3 / 1772 (0.17%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Rectal Haemorrhage				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				

subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatic Cirrhosis			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Bile Duct Stone			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatic Failure			
subjects affected / exposed	2 / 1772 (0.11%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	1 / 1		
Hepatorenal Syndrome			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Hyperbilirubinaemia			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Drug Rash with Eosinophilia and Systemic Symptoms			
subjects affected / exposed	3 / 1772 (0.17%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Eczema			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Erythema				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pruritus				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Purpura				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Rash				
subjects affected / exposed	16 / 1772 (0.90%)			
occurrences causally related to treatment / all	16 / 16			
deaths causally related to treatment / all	0 / 0			
Rash Generalised				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Rash Papular				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Toxic Skin Eruption				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Renal Failure				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Renal Failure Acute				

subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Back Pain			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Arthritis			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bone Pain			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchopneumonia			
subjects affected / exposed	2 / 1772 (0.11%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		

Febrile Infection			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea Infectious			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Intervertebral Discitis			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Oral Candidiasis			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	2 / 1772 (0.11%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Psoas Abscess			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis Acute			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			

subjects affected / exposed	2 / 1772 (0.11%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Tuberculosis				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Skin Infection				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary Tract Infection				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Anorexia				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Dehydration				
subjects affected / exposed	2 / 1772 (0.11%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	1 / 1			
Hypercatabolism				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Diabetic Ketoacidosis				
subjects affected / exposed	1 / 1772 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hyperglycaemia				

subjects affected / exposed	2 / 1772 (0.11%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	1 / 1		
Hyperuricaemia			
subjects affected / exposed	2 / 1772 (0.11%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	3 / 1772 (0.17%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Ketoacidosis			
subjects affected / exposed	1 / 1772 (0.06%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		

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

Non-serious adverse events	Telaprevir + Pegylated Interferon/Ribavirin		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1293 / 1772 (72.97%)		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	933 / 1772 (52.65%)		
occurrences (all)	1435		
Thrombocytopenia			
subjects affected / exposed	126 / 1772 (7.11%)		
occurrences (all)	170		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	151 / 1772 (8.52%)		
occurrences (all)	172		
Gastrointestinal disorders			

Anal Pruritus			
subjects affected / exposed	100 / 1772 (5.64%)		
occurrences (all)	101		
Nausea			
subjects affected / exposed	146 / 1772 (8.24%)		
occurrences (all)	154		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	266 / 1772 (15.01%)		
occurrences (all)	282		
Rash			
subjects affected / exposed	424 / 1772 (23.93%)		
occurrences (all)	500		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 May 2011	The overall reason for the amendment was to change in collection period for serious adverse events (SAEs) and reporting period for pregnancies and the fact that female participants should discontinue treatment if they become pregnant.
16 August 2011	The overall reason for the amendment was to add the collection of an optional blood sample for genotype evaluations of specific genetic markers related to treatment response outcomes and specified adverse events including rash.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported