Clinical trial results:
A Phase 3 Blinded Randomized Study of Peginterferon Lambda-1a and Ribavirin Compared to Peginterferon Alfa-2a and Ribavirin, Each Administered with Telaprevir in Subjects with Genotype-1 Chronic Hepatitis C who are Treatment-naïve or Relapsed on Treatment with Peginterferon Alfa and Ribavirin

Summary

EudraCT number	2011-004695-11
Trial protocol	AT BE CZ GB PL IT ES
Global end of trial date	04 February 2015

Results information

Result version number	v1 (current)
This version publication date	21 May 2016
First version publication date	21 May 2016

Trial information

Trial identification

Sponsor protocol code	AI452-020

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01598090
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Bristol-Myers Squibb International Corporation, Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, clinical.trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, clinical.trials@bms.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	04 February 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 February 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to determine whether Peginterferon Lambda-1a (Lambda) combined with Ribavirin (RBV) and Telaprevir (TVR) is effective in the treatment of chronic Hepatitis C (CHC) compared to Peginterferon Alfa-2a (alfa-2a) combined with RBV and TVR.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 June 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Brazil: 95
Country: Number of subjects enrolled	Canada: 41
Country: Number of subjects enrolled	Israel: 28
Country: Number of subjects enrolled	Russian Federation: 139
Country: Number of subjects enrolled	Switzerland: 5
Country: Number of subjects enrolled	United States: 264
Country: Number of subjects enrolled	Austria: 12
Country: Number of subjects enrolled	Poland: 100
Country: Number of subjects enrolled	Spain: 76
Country: Number of subjects enrolled	United Kingdom: 19
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Czech Republic: 26
Country: Number of subjects enrolled	France: 19
Country: Number of subjects enrolled	Germany: 22
Country: Number of subjects enrolled	Italy: 31
Worldwide total number of subjects	881
EEA total number of subjects	309

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)	851
From 65 to 84 years	30
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 881 subjects were recruited at 98 sites.

Pre-assignment

Screening details:

Out of 881 subjects enrolled, 27 subjects were treated in Part A and 617 subjects were treated in Part B of the study.

Period 1

Period 1 title	Treatment period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Blinding implementation details:

Part A of this study was open-label. In Part B of this study, treatment assignment was site and subject blinded for the entire duration of the study. A designated member of the study staff at the investigative site and a necessary personnel at the Sponsor not directly involved in the assessment of safety in the study was unblinded.

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A: Peginterferon Lambda-1a + RBV + TVR (Open Label)

Arm description:

Subjects with genotype (GT) -1 chronic Hepatitis C virus infection received Peginterferon Lambda-1a 180 mcg subcutaneously, once weekly for 24 or 48 weeks depending on the extended rapid virologic response (eRVR); Ribavirin 1000 or 1200 mg (based on weight) tablets, orally daily in 2 divided doses for 24 or 48 weeks depending on the eRVR response; Telaprevir 750 mg tablets, orally three times a day for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Peginterferon lambda- 1a
Investigational medicinal product code	BMS-914143
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Peginterferon lambda-1a 180 mcg was administered subcutaneously once weekly for 24 or 48 weeks.

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

Dosage and administration details:

Ribavirin 1000 mg total daily dose was administered orally in 2 divided doses as 400 mg in Ante Meridian (AM) and 600 mg in Post Meridian (PM) (for subjects <75 kg) or 1200 mg total daily dose was administered orally in 2 divided doses as 600 mg in AM and PM (for subjects >=75 kg) with meal for 24 or 48 weeks.

Investigational medicinal product name	Telaprevir
Investigational medicinal product code	
Other name	Incivek

Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Telaprevir 750 mg tablets (375 mg*2) were administered orally three times a day for 12 weeks.

Arm title	Part B: Peginterferon Lambda-1a + RBV + TVR

Arm description:

Subjects who were either treatment naive or who were relapsers to previous Peginterferon alfa-2a/ribavirin treatment received Peginterferon Lambda-1a 180 mcg subcutaneously, once weekly for 24 or 48 weeks depending on the extended rapid virologic response (eRVR); Ribavirin 1000 or 1200 mg (based on weight) tablets, orally daily in 2 divided doses for 24 or 48 weeks depending on the eRVR response; Telaprevir 750 mg tablets, orally three times a day for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Peginterferon lambda- 1a
Investigational medicinal product code	BMS-914143
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Peginterferon lambda-1a 180 mcg was administered subcutaneously once weekly for 24 or 48 weeks.

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

Dosage and administration details:

Ribavirin 1000 mg total daily dose was administered orally in 2 divided doses as 400 mg in AM and 600 mg in PM (for subjects <75 kg) or 1200 mg total daily dose was administered orally in 2 divided doses as 600 mg in AM and PM (for subjects >=75 kg) with meal for 24 or 48 weeks.

Investigational medicinal product name	Telaprevir
Investigational medicinal product code	
Other name	Incivek
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Telaprevir 750 mg tablets (375 mg*2) were administered orally three times a day for 12 weeks.

Arm title	Part B: Peginterferon Alfa-2a + RBV + TVR

Arm description:

Subjects who were either treatment naive or who were relapsers to previous Peginterferon alfa-2a/ribavirin treatment received Peginterferon alfa-2a 180 mcg subcutaneously, once weekly for 24 or 48 weeks depending on the extended rapid virologic response (eRVR); Ribavirin 1000 or 1200 mg (based on weight) tablets, orally daily in 2 divided doses for 24 or 48 weeks depending on the eRVR response; Telaprevir 750 mg tablets, orally three times a day for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Peginterferon alfa- 2a
Investigational medicinal product code	
Other name	Pegasys
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Peginterferon alfa-2a 180 mcg was administered subcutaneously once weekly for 24 or 48 weeks.

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

Dosage and administration details:

Ribavirin 1000 mg total daily dose was administered orally in 2 divided doses as 400 mg in AM and 600 mg in PM (for subjects <75 kg) or 1200 mg total daily dose was administered orally in 2 divided doses as 600 mg in AM and PM (for subjects >=75 kg) with meal for 24 or 48 weeks.

Investigational medicinal product name	Telaprevir
Investigational medicinal product code	
Other name	Incivek
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Telaprevir 750 mg tablets (375 mg*2) were administered orally three times a day for 12 weeks.

Number of subjects in period 1[1]	Part A: Peginterferon Lambda-1a + RBV + TVR (Open Label)	Part B: Peginterferon Lambda-1a + RBV + TVR	Part B: Peginterferon Alfa-2a + RBV + TVR
Started	27	411	206
Completed	16	339	171
Not completed	11	72	35
Consent withdrawn by subject	-	4	3
Adverse event, non-fatal	2	33	17
Other reasons	-	4	1
Lost to follow-up	1	5	1
Poor/non-compliance	-	2	-
Subject no longer meets study criteria	-	1	-
Subject requested to discontinue study treatment	3	9	7
Lack of efficacy	5	14	6

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Out of 881 subjects who were enrolled, 648 were randomised and only 644 were treated.

Period 2

Period 2 title	Follow-up period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Blinding implementation details:

Part A of this study was open-label. In Part B of this study, treatment assignment will be site and subject blinded for the entire duration of the study. A designated member of the study staff at the

investigative site and a necessary personnel at the Sponsor not directly involved in the assessment of safety in the study was unblinded.

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A: Peginterferon Lambda-1a + RBV + TVR (Open Label)

Arm description:

Subjects were followed up for 48 weeks who received treatment as: Peginterferon Lambda-1a 180 mcg subcutaneously, once weekly for 24 or 48 weeks depending on the extended rapid virologic response (eRVR); Ribavirin 1000 or 1200 mg (based on weight) tablets, orally daily in 2 divided doses for 24 or 48 weeks depending on the eRVR response; Telaprevir 750 mg tablets, orally three times a day for 12 weeks.

Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Part B: Peginterferon Lambda-1a + RBV + TVR

Arm description:

Subjects were followed up for 48 weeks who received treatment as: Peginterferon Lambda-1a 180 mcg subcutaneously, once weekly for 24 or 48 weeks depending on the extended rapid virologic response (eRVR); Ribavirin 1000 or 1200 mg (based on weight) tablets, orally daily in 2 divided doses for 24 or 48 weeks depending on the eRVR response; Telaprevir 750 mg tablets, orally three times a day for 12 weeks.

Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Part B: Peginterferon alfa-2a + RBV + TVR

Arm description:

Subjects were followed up for 48 weeks who received treatment as: Peginterferon alfa-2a 180 mcg subcutaneously, once weekly for 24 or 48 weeks depending on the extended rapid virologic response (eRVR); Ribavirin 1000 or 1200 mg (based on weight) tablets, orally daily in 2 divided doses for 24 or 48 weeks depending on the eRVR response; Telaprevir 750 mg tablets, orally three times a day for 12 weeks.

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 2	Part A: Peginterferon Lambda-1a + RBV + TVR (Open Label)	Part B: Peginterferon Lambda-1a + RBV + TVR	Part B: Peginterferon alfa-2a + RBV + TVR
Started	16	339	171
Completed	21	364	171
Not completed	5	35	28
Consent withdrawn by subject	-	3	2
Death	-	1	-
Not reported	-	10	4
Other reasons	2	8	8
Follow-up no longer required per protocol	1	3	2
Lost to follow-up	2	10	12
Joined	10	60	28

Re-joined for follow-up	10	60	28

Baseline characteristics

Reporting groups

Reporting group title	Part A: Peginterferon Lambda-1a + RBV + TVR (Open Label)

Reporting group description:

Subjects with genotype (GT) -1 chronic Hepatitis C virus infection received Peginterferon Lambda-1a 180 mcg subcutaneously, once weekly for 24 or 48 weeks depending on the extended rapid virologic response (eRVR); Ribavirin 1000 or 1200 mg (based on weight) tablets, orally daily in 2 divided doses for 24 or 48 weeks depending on the eRVR response; Telaprevir 750 mg tablets, orally three times a day for 12 weeks.

Reporting group title	Part B: Peginterferon Lambda-1a + RBV + TVR

Reporting group description:

Subjects who were either treatment naive or who were relapsers to previous Peginterferon alfa-2a/ribavirin treatment received Peginterferon Lambda-1a 180 mcg subcutaneously, once weekly for 24 or 48 weeks depending on the extended rapid virologic response (eRVR); Ribavirin 1000 or 1200 mg (based on weight) tablets, orally daily in 2 divided doses for 24 or 48 weeks depending on the eRVR response; Telaprevir 750 mg tablets, orally three times a day for 12 weeks.

Reporting group title	Part B: Peginterferon Alfa-2a + RBV + TVR

Reporting group description:

Subjects who were either treatment naive or who were relapsers to previous Peginterferon alfa-2a/ribavirin treatment received Peginterferon alfa-2a 180 mcg subcutaneously, once weekly for 24 or 48 weeks depending on the extended rapid virologic response (eRVR); Ribavirin 1000 or 1200 mg (based on weight) tablets, orally daily in 2 divided doses for 24 or 48 weeks depending on the eRVR response; Telaprevir 750 mg tablets, orally three times a day for 12 weeks.

Reporting group values	Part A: Peginterferon Lambda-1a + RBV + TVR (Open Label)	Part B: Peginterferon Lambda-1a + RBV + TVR	Part B: Peginterferon Alfa-2a + RBV + TVR
Number of subjects	27	411	206
Age categorical Units: Subjects			
<21	0	5	2
21 - <65	27	392	197
>=65	0	14	7
Age continuous Units: years			
arithmetic mean	51.9	45.8	45
standard deviation	± 8.62	± 12.42	± 12.19
Gender categorical Units: Subjects			
Female	9	152	80
Male	18	259	126

Reporting group values	Total		
Number of subjects	644		
Age categorical Units: Subjects			
<21	7		
21 - <65	616		

>=65	21		

Age continuous Units: years arithmetic mean standard deviation	- 		
Gender categorical Units: Subjects			
Female	241		
Male	403		

End points

End points reporting groups

Reporting group title	Part A: Peginterferon Lambda-1a + RBV + TVR (Open Label)

Reporting group description:

Subjects with genotype (GT) -1 chronic Hepatitis C virus infection received Peginterferon Lambda-1a 180 mcg subcutaneously, once weekly for 24 or 48 weeks depending on the extended rapid virologic response (eRVR); Ribavirin 1000 or 1200 mg (based on weight) tablets, orally daily in 2 divided doses for 24 or 48 weeks depending on the eRVR response; Telaprevir 750 mg tablets, orally three times a day for 12 weeks.

Reporting group title	Part B: Peginterferon Lambda-1a + RBV + TVR

Reporting group description:

Subjects who were either treatment naive or who were relapsers to previous Peginterferon alfa-2a/ribavirin treatment received Peginterferon Lambda-1a 180 mcg subcutaneously, once weekly for 24 or 48 weeks depending on the extended rapid virologic response (eRVR); Ribavirin 1000 or 1200 mg (based on weight) tablets, orally daily in 2 divided doses for 24 or 48 weeks depending on the eRVR response; Telaprevir 750 mg tablets, orally three times a day for 12 weeks.

Reporting group title	Part B: Peginterferon Alfa-2a + RBV + TVR

Reporting group description:

Subjects who were either treatment naive or who were relapsers to previous Peginterferon alfa-2a/ribavirin treatment received Peginterferon alfa-2a 180 mcg subcutaneously, once weekly for 24 or 48 weeks depending on the extended rapid virologic response (eRVR); Ribavirin 1000 or 1200 mg (based on weight) tablets, orally daily in 2 divided doses for 24 or 48 weeks depending on the eRVR response; Telaprevir 750 mg tablets, orally three times a day for 12 weeks.

Reporting group title	Part A: Peginterferon Lambda-1a + RBV + TVR (Open Label)

Reporting group description:

Subjects were followed up for 48 weeks who received treatment as: Peginterferon Lambda-1a 180 mcg subcutaneously, once weekly for 24 or 48 weeks depending on the extended rapid virologic response (eRVR); Ribavirin 1000 or 1200 mg (based on weight) tablets, orally daily in 2 divided doses for 24 or 48 weeks depending on the eRVR response; Telaprevir 750 mg tablets, orally three times a day for 12 weeks.

Reporting group title	Part B: Peginterferon Lambda-1a + RBV + TVR

Reporting group description:

Subjects were followed up for 48 weeks who received treatment as: Peginterferon Lambda-1a 180 mcg subcutaneously, once weekly for 24 or 48 weeks depending on the extended rapid virologic response (eRVR); Ribavirin 1000 or 1200 mg (based on weight) tablets, orally daily in 2 divided doses for 24 or 48 weeks depending on the eRVR response; Telaprevir 750 mg tablets, orally three times a day for 12 weeks.

Reporting group title	Part B: Peginterferon alfa-2a + RBV + TVR

Reporting group description:

Subjects were followed up for 48 weeks who received treatment as: Peginterferon alfa-2a 180 mcg subcutaneously, once weekly for 24 or 48 weeks depending on the extended rapid virologic response (eRVR); Ribavirin 1000 or 1200 mg (based on weight) tablets, orally daily in 2 divided doses for 24 or 48 weeks depending on the eRVR response; Telaprevir 750 mg tablets, orally three times a day for 12 weeks.

Primary: Percentage of Subjects With Extended Rapid Virologic Response (eRVR) - Part A

End point title	Percentage of Subjects With Extended Rapid Virologic Response (eRVR) - Part A[1][2]

End point description:

eRVR was defined as Hepatitis C virus (HCV) RNA level below the lower limit of quantitation, target not detected at Weeks 4 and 12 of treatment. HCV RNA level was measured using the Roche COBAS® TaqMan HCV Test v.2.0 (lower limit of quantitation =25 IU/mL; limit of detection ~ 10 IU/mL). The analysis was performed using Modified Intent-to-Treat method, defined as the proportions of subjects meeting the response criteria in numerator and denominator based on all treated subjects. The analysis was performed in all treated subjects.

End point type	Primary

End point timeframe:

Week 4 and Week 12

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive summary statistics were planned for this outcome measure.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was planned to evaluate for the specified arm only.

End point values	Part A: Peginterferon Lambda-1a + RBV + TVR (Open Label)			
Subject group type	Reporting group			
Number of subjects analysed	27			
Units: Percentage of subjects				
number (confidence interval 95%)	51.9 (31.9 to 71.3)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Sustained Virologic Response at Follow-up Week 12 (SVR12) - Part B

End point title	Percentage of Subjects With Sustained Virologic Response at Follow-up Week 12 (SVR12) - Part B[3]

End point description:

SVR12 was defined as Hepatitis C virus (HCV) RNA level below lower limit of quantitation, target detected or not detected at Week 12 of post-treatment follow-up. HCV RNA level was measured using the Roche COBAS® TaqMan HCV Test v.2.0 (lower limit of quantitation =25 IU/mL; limit of detection ~ 10 IU/mL). The analysis was performed using Modified Intent-to-Treat method defined as the proportions of subjects meeting the response criteria in numerator and denominator based on all treated subjects. The analysis was performed in all treated subjects.

End point type	Primary

End point timeframe:

Follow-up Week 12

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was planned to evaluate for the specified arm only.

End point values	Part B: Peginterferon Lambda-1a + RBV + TVR	Part B: Peginterferon Alfa-2a + RBV + TVR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	411	206		
Units: Percentage of subjects				
number (confidence interval 95%)	76.2 (72 to 80.3)	82 (76.8 to 87.3)		

Statistical analyses

Statistical analysis title	Comparison of SVR12
Comparison groups	Part B: Peginterferon Lambda-1a + RBV + TVR v Part B: Peginterferon Alfa-2a + RBV + TVR
Number of subjects included in analysis	617
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
P-value	= 99999 [5]
Method	Mantel-Haenszel
Parameter estimate	Difference in proportions
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.3
upper limit	0.8

Notes:

[4] - Non-inferiority of Lambda/RBV/TVR to Alfa/RBV/TVR was not established because the lower limit of the 95% CI was less than the predefined non-inferiority margin of -12%. As a result, key secondary endpoints were not tested hierarchically to compare treatment groups.

[5] - Non-inferiority testing is based on lower limit of confidence interval.

Primary: Number of Subjects With Adverse Events (AEs), Serious Adverse Events (SAEs), Drug Related AEs, Discontinuation due to AEs, Dose Reductions and Death - Part A

End point title	Number of Subjects With Adverse Events (AEs), Serious Adverse Events (SAEs), Drug Related AEs, Discontinuation due to AEs, Dose Reductions and Death - Part A[6][7]

End point description:

An AE was defined as any new untoward medical occurrence or worsening of a pre-existing medical condition in a subject or clinical investigation subject administered an investigational (medicinal) product. An SAE was defined as any untoward medical occurrence that at any dose resulted in death, was life-threatening, required inpatient hospitalization or caused prolongation of existing hospitalization. Safety analysis included all treated subjects.

End point type	Primary

End point timeframe:

Day 1 of treatment up to Week 48

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: Only descriptive summary statistics were planned for this outcome measure.

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was planned to evaluate for the specified arm only.

End point values	Part A: Peginterferon Lambda-1a + RBV + TVR (Open Label)			
Subject group type	Reporting group			
Number of subjects analysed	27			
Units: Subjects				
AEs	26			
SAEs	6			
Drug related AEs	12			
Discontinuation due to AEs	2			
Death	0			
Dose reductions - Lambda	3			
Dose reductions - RBV	7			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Sustained Virologic Response at Follow-up Week 12 (SVR12) - Part A

End point title	Percentage of Subjects With Sustained Virologic Response at Follow-up Week 12 (SVR12) - Part A[8]

End point description:

SVR12 was defined as Hepatitis C virus (HCV) RNA level below lower limit of quantitation (LLOQ), target detected or not detected at Week 12 of post-treatment follow-up. HCV RNA level was measured using the Roche COBAS® TaqMan HCV Test v.2.0 (LLOQ =25 IU/mL; limit of detection ~ 10 IU/mL). The analysis was performed using Modified Intent-to-Treat method defined as the proportions of subjects meeting the response criteria in numerator and denominator based on all treated subjects. The analysis was performed in all treated subjects.

End point type	Secondary

End point timeframe:

Follow-up Week 12

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was planned to evaluate for the specified arm only.

End point values	Part A: Peginterferon Lambda-1a + RBV + TVR (Open Label)			
Subject group type	Reporting group			
Number of subjects analysed	27			
Units: Percentage of subjects				
number (confidence interval 95%)	48.1 (28.7 to 68.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Sustained Virologic Response at Follow-up Week 24 (SVR24) - Part A

End point title	Percentage of Subjects With Sustained Virologic Response at Follow-up Week 24 (SVR24) - Part A[9]

End point description:

SVR24 was defined as Hepatitis C virus (HCV) RNA level below lower limit of quantitation (LLOQ), target detected or not detected at Week 24 of post-treatment follow-up. HCV RNA level was measured using the Roche COBAS® TaqMan HCV Test v.2.0 (LLOQ) =25 IU/mL; limit of detection ~ 10 IU/mL). The analysis was performed using Modified Intent-to-Treat method defined as the proportions of subjects meeting the response criteria in numerator and denominator based on all treated subjects. The analysis was performed in all treated subjects.

End point type	Secondary

End point timeframe:

Follow-up Week 24

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was planned to evaluate for the specified arm only.

End point values	Part A: Peginterferon Lambda-1a + RBV + TVR (Open Label)			
Subject group type	Reporting group			
Number of subjects analysed	27			
Units: Percentage of subjects				
number (confidence interval 95%)	40.7 (22.4 to 61.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Treatment-Naive Subjects With Sustained Virologic Response at Follow-up Week 12 (SVR12) - Part B

End point title	Percentage of Treatment-Naive Subjects With Sustained Virologic Response at Follow-up Week 12 (SVR12) - Part B[10]

End point description:

SVR12 was defined as Hepatitis C virus (HCV) RNA level below lower limit of quantitation (LLOQ), target detected or not detected at Week 12 of post-treatment follow-up. HCV RNA level were measured using the Roche COBAS® TaqMan HCV Test v.2.0 (LLOQ =25 IU/mL; limit of detection ~ 10 IU/mL). The analysis was performed using Modified Intent-to-Treat method defined as the proportions of subjects meeting the response criteria in numerator and denominator based on all treated subjects. The analysis was performed in all the treatment-naive treated subjects.

End point type	Secondary

End point timeframe:

Follow-up Week 12

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was planned to evaluate for the specified arm only.

End point values	Part B: Peginterferon Lambda-1a + RBV + TVR	Part B: Peginterferon Alfa-2a + RBV + TVR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	311	155		
Units: Percentage of subjects				
number (confidence interval 95%)	73.6 (68.7 to 78.5)	81.9 (75.9 to 88)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Treatment Emergent Cytopenic Abnormalities - Part B

End point title	Percentage of Subjects With Treatment Emergent Cytopenic Abnormalities - Part B[11]

End point description:

Cytopenic abnormalities included anemia defined as hemoglobin <10 grams/decilitre; neutropenia defined as Absolute neutrophil count (ANC) <750 cubic millimetre (mm^3); thrombocytopenia defined as platelets <50,000 mm^3. The analysis was performed using Modified Intent-to-Treat method, defined as the proportions of subjects with abnormalities in numerator and denominator based on all treated subjects. The analysis was performed in all treated subjects.

End point type	Secondary

End point timeframe:

After Day 1 of treatment up to Week 48

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was planned to evaluate for the specified arm only.

End point values	Part B: Peginterferon Lambda-1a + RBV + TVR	Part B: Peginterferon Alfa-2a + RBV + TVR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	411	206		
Units: Percentage of subjects				
number (confidence interval 95%)	11.7 (8.6 to 14.8)	55.8 (49 to 62.6)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Subjects With Extended Rapid Virologic Response (eRVR) - Part B[12]

End point description:

eRVR was defined as Hepatitis C virus (HCV) RNA level below the lower limit of quantitation, target not detected at Weeks 4 and 12 of treatment. HCV RNA level was measured using the Roche COBAS® TaqMan HCV Test v.2.0 (lower limit of quantitation =25 IU/mL; limit of detection ~ 10 IU/mL). The analysis was performed using Modified Intent-to-Treat method defined as the proportions of subjects meeting the response criteria in numerator and denominator based on all treated subjects. The analysis was performed in all treated subjects.

End point type	Secondary

End point timeframe:

Week 4 and Week 12

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was planned to evaluate for the specified arm only.

End point values	Part B: Peginterferon Lambda-1a + RBV + TVR	Part B: Peginterferon Alfa-2a + RBV + TVR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	411	206		
Units: Percentage of subjects				
number (confidence interval 95%)	64 (59.3 to 68.6)	70.9 (64.7 to 77.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With On-Treatment Flu-Like Symptoms And Musculoskeletal Symptoms- Part B

End point title	Percentage of Subjects With On-Treatment Flu-Like Symptoms And Musculoskeletal Symptoms- Part B[13]

End point description:

Flu-like symptoms included pyrexia, chills, and pain. Musculoskeletal symptoms included arthralgia, myalgia, and back pain. The analysis was performed using Modified Intent-to-Treat method, defined as the proportions of subjects with symptoms in numerator and denominator based on all treated subjects. The analysis was performed in all treated subjects.

End point type	Secondary

End point timeframe:

After Day 1 of treatment up to Week 48

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was planned to evaluate for the specified arm only.

End point values	Part B: Peginterferon Lambda-1a + RBV + TVR	Part B: Peginterferon Alfa-2a + RBV + TVR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	411	206		
Units: Percentage of subjects				

number (confidence interval 95%)				
Flu-Like Symptoms	14.4 (11 to 17.7)	36.4 (29.8 to 43)		
Musculoskeletal symptoms	21.4 (17.4 to 25.4)	30.6 (24.3 to 36.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Sustained Virologic Response at Follow-up Week 24 (SVR24) - Part B

End point title	Percentage of Subjects With Sustained Virologic Response at Follow-up Week 24 (SVR24) - Part B[14]

End point description:

SVR24 was defined as Hepatitis C virus (HCV) RNA level below lower limit of quantitation (LLOQ), target detected or not detected at Week 24 of post-treatment follow-up. HCV RNA level was measured using the Roche COBAS® TaqMan HCV Test v.2.0 (LLOQ) =25 IU/mL; limit of detection ~ 10 IU/mL). The analysis was performed using Observed value method, defined as the proportions of subjects meeting the response criteria in numerator and denominator based on all treated subjects with HCV RNA measured at follow-up Week 24. The analysis was performed in all treated subjects with HCV RNA measured at follow-up Week 24 instead of all treated subjects due to early study termination.

End point type	Secondary

End point timeframe:

Follow-up Week 24

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was planned to evaluate for the specified arm only.

End point values	Part B: Peginterferon Lambda-1a + RBV + TVR	Part B: Peginterferon Alfa-2a + RBV + TVR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	223	108		
Units: Percentage of subjects				
number (confidence interval 95%)	83 (78 to 87.9)	87 (80.7 to 93.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Rash

End point title	Percentage of Subjects With Rash

End point description:

All skin reactions involving rash or rash-like events that occurred on treatment were reported. The analysis was performed in all treated subjects.

End point type	Secondary

End point timeframe:

Day 1 of treatment up to Week 48

End point values	Part A: Peginterferon Lambda-1a + RBV + TVR (Open Label)	Part B: Peginterferon Lambda-1a + RBV + TVR	Part B: Peginterferon Alfa-2a + RBV + TVR	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	27	411	206	
Units: Percentage of subjects				
number (not applicable)	63	36.3	38.3	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 of treatment up to Week 48

Adverse event reporting additional description:

On-Treatment period

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Part A: Peginterferon Lambda-1a + RBV + TVR (Open Label)

Reporting group description:

Subjects with genotype (GT) -1 chronic Hepatitis C virus infection received Peginterferon Lambda-1a 180 mcg subcutaneously, once weekly for 24 or 48 weeks depending on the extended rapid virologic response (eRVR); Ribavirin 1000 or 1200 mg (based on weight) tablets, orally daily in 2 divided doses for 24 or 48 weeks depending on the eRVR response; Telaprevir 750 mg tablets, orally three times a day for 12 weeks.

Reporting group title	Part B: Peginterferon Lambda-1a + RBV + TVR

Reporting group description:

Subjects who were either treatment naive or who were relapsers to previous Peginterferon alfa-2a/ribavirin treatment received Peginterferon Lambda-1a 180 mcg subcutaneously, once weekly for 24 or 48 weeks depending on the extended rapid virologic response (eRVR); Ribavirin 1000 or 1200 mg (based on weight) tablets, orally daily in 2 divided doses for 24 or 48 weeks depending on response (eRVR); Telaprevir 750 mg tablets, orally three times a day for 12 weeks.

Reporting group title	Part B: Peginterferon Alfa-2a + RBV + TVR

Reporting group description:

Subjects who were either treatment naive or who were relapsers to previous Peginterferon alfa-2a/ribavirin treatment received Peginterferon alfa-2a 180 mcg subcutaneously, once weekly for 24 or 48 weeks depending on the extended rapid virologic response (eRVR); Ribavirin 1000 or 1200 mg (based on weight) tablets, orally daily in 2 divided doses for 24 or 48 weeks depending on the eRVR response; Telaprevir 750 mg tablets, orally three times a day for 12 weeks.

Serious adverse events	Part A: Peginterferon Lambda-1a + RBV + TVR (Open Label)	Part B: Peginterferon Lambda-1a + RBV + TVR	Part B: Peginterferon Alfa-2a + RBV + TVR
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 27 (22.22%)	43 / 411 (10.46%)	20 / 206 (9.71%)
number of deaths (all causes)	0	1	1
number of deaths resulting from adverse events	0	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 27 (0.00%)	1 / 411 (0.24%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration			

site conditions			
Strangulated hernia			
subjects affected / exposed	0 / 27 (0.00%)	1 / 411 (0.24%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 27 (0.00%)	0 / 411 (0.00%)	2 / 206 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 411 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Psychiatric disorders			
Substance-induced psychotic disorder			
subjects affected / exposed	0 / 27 (0.00%)	0 / 411 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 27 (0.00%)	1 / 411 (0.24%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 27 (0.00%)	1 / 411 (0.24%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 27 (0.00%)	1 / 411 (0.24%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrocardiogram QT prolonged			

subjects affected / exposed	0 / 27 (0.00%)	1 / 411 (0.24%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic enzyme increased			
subjects affected / exposed	0 / 27 (0.00%)	1 / 411 (0.24%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	0 / 27 (0.00%)	1 / 411 (0.24%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic enzymes increased			
subjects affected / exposed	0 / 27 (0.00%)	1 / 411 (0.24%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carotid bruit			
subjects affected / exposed	0 / 27 (0.00%)	0 / 411 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	1 / 27 (3.70%)	1 / 411 (0.24%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 27 (0.00%)	1 / 411 (0.24%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 27 (0.00%)	0 / 411 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 27 (0.00%)	1 / 411 (0.24%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Demyelination			
subjects affected / exposed	0 / 27 (0.00%)	0 / 411 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 27 (0.00%)	1 / 411 (0.24%)	3 / 206 (1.46%)
occurrences causally related to treatment / all	0 / 0	1 / 1	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 411 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Ocular icterus			
subjects affected / exposed	0 / 27 (0.00%)	3 / 411 (0.73%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 27 (3.70%)	0 / 411 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peptic ulcer haemorrhage			
subjects affected / exposed	1 / 27 (3.70%)	0 / 411 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			

subjects affected / exposed	0 / 27 (0.00%)	2 / 411 (0.49%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 27 (0.00%)	1 / 411 (0.24%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 27 (0.00%)	1 / 411 (0.24%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 27 (0.00%)	1 / 411 (0.24%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 411 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 27 (0.00%)	0 / 411 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal vascular malformation			
subjects affected / exposed	0 / 27 (0.00%)	0 / 411 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	3 / 27 (11.11%)	11 / 411 (2.68%)	2 / 206 (0.97%)
occurrences causally related to treatment / all	2 / 3	11 / 11	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-induced liver injury			

subjects affected / exposed	0 / 27 (0.00%)	4 / 411 (0.97%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	4 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatotoxicity			
subjects affected / exposed	0 / 27 (0.00%)	2 / 411 (0.49%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertransaminasaemia			
subjects affected / exposed	0 / 27 (0.00%)	2 / 411 (0.49%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice cholestatic			
subjects affected / exposed	0 / 27 (0.00%)	2 / 411 (0.49%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 27 (0.00%)	1 / 411 (0.24%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 27 (0.00%)	1 / 411 (0.24%)	5 / 206 (2.43%)
occurrences causally related to treatment / all	0 / 0	1 / 1	5 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug reaction with eosinophilia and systemic symptoms			
subjects affected / exposed	0 / 27 (0.00%)	0 / 411 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 27 (0.00%)	1 / 411 (0.24%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 27 (0.00%)	1 / 411 (0.24%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 27 (0.00%)	1 / 411 (0.24%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

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

Non-serious adverse events	Part A: Peginterferon Lambda-1a + RBV + TVR (Open Label)	Part B: Peginterferon Lambda-1a + RBV + TVR	Part B: Peginterferon Alfa-2a + RBV + TVR
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 27 (96.30%)	369 / 411 (89.78%)	197 / 206 (95.63%)
Investigations			
Amylase increased			
subjects affected / exposed	0 / 27 (0.00%)	21 / 411 (5.11%)	3 / 206 (1.46%)
occurrences (all)	0	26	5
Blood bilirubin increased			
subjects affected / exposed	2 / 27 (7.41%)	19 / 411 (4.62%)	2 / 206 (0.97%)
occurrences (all)	3	25	2
Alanine aminotransferase increased			
subjects affected / exposed	2 / 27 (7.41%)	30 / 411 (7.30%)	1 / 206 (0.49%)
occurrences (all)	2	33	2
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 27 (3.70%)	30 / 411 (7.30%)	1 / 206 (0.49%)
occurrences (all)	1	38	2
Bilirubin conjugated increased			
subjects affected / exposed	2 / 27 (7.41%)	6 / 411 (1.46%)	1 / 206 (0.49%)
occurrences (all)	2	9	1
Nervous system disorders			

Headache			
subjects affected / exposed	8 / 27 (29.63%)	66 / 411 (16.06%)	42 / 206 (20.39%)
occurrences (all)	9	76	54
Dizziness			
subjects affected / exposed	2 / 27 (7.41%)	52 / 411 (12.65%)	24 / 206 (11.65%)
occurrences (all)	2	55	33
Dysgeusia			
subjects affected / exposed	3 / 27 (11.11%)	11 / 411 (2.68%)	9 / 206 (4.37%)
occurrences (all)	3	11	11
Syncope			
subjects affected / exposed	2 / 27 (7.41%)	5 / 411 (1.22%)	1 / 206 (0.49%)
occurrences (all)	2	5	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	16 / 27 (59.26%)	143 / 411 (34.79%)	75 / 206 (36.41%)
occurrences (all)	16	162	92
Asthenia			
subjects affected / exposed	0 / 27 (0.00%)	81 / 411 (19.71%)	61 / 206 (29.61%)
occurrences (all)	0	95	69
Pyrexia			
subjects affected / exposed	2 / 27 (7.41%)	31 / 411 (7.54%)	53 / 206 (25.73%)
occurrences (all)	2	37	61
Influenza like illness			
subjects affected / exposed	3 / 27 (11.11%)	26 / 411 (6.33%)	36 / 206 (17.48%)
occurrences (all)	4	29	39
Chills			
subjects affected / exposed	1 / 27 (3.70%)	35 / 411 (8.52%)	35 / 206 (16.99%)
occurrences (all)	1	42	41
Injection site reaction			
subjects affected / exposed	4 / 27 (14.81%)	7 / 411 (1.70%)	6 / 206 (2.91%)
occurrences (all)	4	7	6
Pain			
subjects affected / exposed	2 / 27 (7.41%)	6 / 411 (1.46%)	6 / 206 (2.91%)
occurrences (all)	2	6	6
Oedema peripheral			

subjects affected / exposed	2 / 27 (7.41%)	15 / 411 (3.65%)	3 / 206 (1.46%)
occurrences (all)	2	16	3
Injection site rash			
subjects affected / exposed	3 / 27 (11.11%)	6 / 411 (1.46%)	0 / 206 (0.00%)
occurrences (all)	3	6	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 27 (11.11%)	53 / 411 (12.90%)	100 / 206 (48.54%)
occurrences (all)	3	55	111
Neutropenia			
subjects affected / exposed	0 / 27 (0.00%)	10 / 411 (2.43%)	35 / 206 (16.99%)
occurrences (all)	0	17	45
Leukopenia			
subjects affected / exposed	0 / 27 (0.00%)	9 / 411 (2.19%)	32 / 206 (15.53%)
occurrences (all)	0	13	41
Thrombocytopenia			
subjects affected / exposed	0 / 27 (0.00%)	1 / 411 (0.24%)	17 / 206 (8.25%)
occurrences (all)	0	2	22
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	11 / 27 (40.74%)	172 / 411 (41.85%)	67 / 206 (32.52%)
occurrences (all)	12	195	78
Diarrhoea			
subjects affected / exposed	13 / 27 (48.15%)	61 / 411 (14.84%)	37 / 206 (17.96%)
occurrences (all)	13	70	43
Vomiting			
subjects affected / exposed	5 / 27 (18.52%)	66 / 411 (16.06%)	25 / 206 (12.14%)
occurrences (all)	5	93	29
Anal pruritus			
subjects affected / exposed	4 / 27 (14.81%)	59 / 411 (14.36%)	22 / 206 (10.68%)
occurrences (all)	4	64	22
Anorectal discomfort			
subjects affected / exposed	5 / 27 (18.52%)	28 / 411 (6.81%)	17 / 206 (8.25%)
occurrences (all)	5	30	18
Dyspepsia			

subjects affected / exposed	2 / 27 (7.41%)	28 / 411 (6.81%)	13 / 206 (6.31%)
occurrences (all)	2	30	17
Haemorrhoids			
subjects affected / exposed	1 / 27 (3.70%)	17 / 411 (4.14%)	11 / 206 (5.34%)
occurrences (all)	1	17	11
Proctalgia			
subjects affected / exposed	2 / 27 (7.41%)	8 / 411 (1.95%)	5 / 206 (2.43%)
occurrences (all)	2	9	6
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 27 (7.41%)	31 / 411 (7.54%)	37 / 206 (17.96%)
occurrences (all)	2	34	41
Cough			
subjects affected / exposed	3 / 27 (11.11%)	12 / 411 (2.92%)	24 / 206 (11.65%)
occurrences (all)	3	13	27
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	3 / 27 (11.11%)	44 / 411 (10.71%)	4 / 206 (1.94%)
occurrences (all)	3	56	4
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	13 / 27 (48.15%)	187 / 411 (45.50%)	100 / 206 (48.54%)
occurrences (all)	13	209	126
Rash			
subjects affected / exposed	12 / 27 (44.44%)	123 / 411 (29.93%)	57 / 206 (27.67%)
occurrences (all)	13	131	62
Dry skin			
subjects affected / exposed	1 / 27 (3.70%)	52 / 411 (12.65%)	27 / 206 (13.11%)
occurrences (all)	1	56	27
Alopecia			
subjects affected / exposed	1 / 27 (3.70%)	9 / 411 (2.19%)	23 / 206 (11.17%)
occurrences (all)	1	9	24
Rash generalised			
subjects affected / exposed	5 / 27 (18.52%)	4 / 411 (0.97%)	2 / 206 (0.97%)
occurrences (all)	5	4	2
Skin exfoliation			

subjects affected / exposed	2 / 27 (7.41%)	4 / 411 (0.97%)	2 / 206 (0.97%)
occurrences (all)	2	4	2
Psychiatric disorders			
Insomnia			
subjects affected / exposed	8 / 27 (29.63%)	102 / 411 (24.82%)	56 / 206 (27.18%)
occurrences (all)	8	110	63
Anxiety			
subjects affected / exposed	0 / 27 (0.00%)	13 / 411 (3.16%)	11 / 206 (5.34%)
occurrences (all)	0	14	11
Depression			
subjects affected / exposed	5 / 27 (18.52%)	25 / 411 (6.08%)	11 / 206 (5.34%)
occurrences (all)	6	26	11
Irritability			
subjects affected / exposed	3 / 27 (11.11%)	33 / 411 (8.03%)	8 / 206 (3.88%)
occurrences (all)	3	40	8
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 27 (3.70%)	49 / 411 (11.92%)	43 / 206 (20.87%)
occurrences (all)	1	58	55
Myalgia			
subjects affected / exposed	4 / 27 (14.81%)	49 / 411 (11.92%)	43 / 206 (20.87%)
occurrences (all)	4	61	56
Muscle spasms			
subjects affected / exposed	4 / 27 (14.81%)	14 / 411 (3.41%)	2 / 206 (0.97%)
occurrences (all)	4	14	2
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	2 / 27 (7.41%)	3 / 411 (0.73%)	4 / 206 (1.94%)
occurrences (all)	2	4	4
Gastroenteritis			
subjects affected / exposed	2 / 27 (7.41%)	5 / 411 (1.22%)	2 / 206 (0.97%)
occurrences (all)	2	5	2
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 27 (3.70%)	85 / 411 (20.68%)	42 / 206 (20.39%)
occurrences (all)	1	93	47

Hyperuricaemia subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	32 / 411 (7.79%) 43	11 / 206 (5.34%) 11

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 February 2013	The main purpose of this amendment was to clarify primary and secondary objectives, study design, statistical objectives for Part A and Part B of the study, change of medical monitor and study director.
19 June 2013	The purpose of this amendment was to clarify the duration of treatment for all cirrhotics is 48 weeks, stratification applies for all subjects, inclusion/exclusion criteria, the rash management plan for telaprevir, that Hepatitis C virus RNA results was made available to sites and staff at the end of treatment and during follow-up, and the analysis of the secondary endpoint for Part A was for all subjects in Part A.

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.

The study was terminated early as further development of Lambda was terminated, due to the recent approvals of all-oral Hepatitis C virus treatment regimens.

Notes: