Clinical trial results:
A DOUBLE-BLINDED, RANDOMIZED CONTROL STUDY EVALUATING THE EFFICACY AND SAFETY OF PEGINTERFERON LAMBDA-1a COMPARED TO PEGINTERFERON ALFA-2a, EACH IN COMBINATION WITH RIBAVARIN, IN THE TREATMENT OF NAIVE GENOTYPE 1 CHRONIC HEPATITIS C SUBJECTS

Summary

EudraCT number	2012-003508-11
Trial protocol	CZ PL
Global end of trial date	18 September 2014

Results information

Result version number	v1 (current)
This version publication date	29 December 2018
First version publication date	29 December 2018

Trial information

Trial identification

Sponsor protocol code	AI452033

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, clinical.trails@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trails@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	18 September 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 September 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Evaluation of the safety of 48 weeks of treatment with Lambda/RBV compared to Alfa-2a/RBV in reducing an aggregate of treatment emergent cytopenic abnormalities (anemia as defined by hemoglobin [Hb] <10 g/dL, and/or neutropenia as defined by ANC <750 mm3 and/or thrombocytopenia as defined by platelets <50,000 mm3)

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	08 April 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Korea, Republic of: 19
Country: Number of subjects enrolled	Mexico: 20
Worldwide total number of subjects	39
EEA total number of subjects	0

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)	36
From 65 to 84 years	3

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

76 subjects were enrolled; 40 subjects were randomized and received treatment; 36 subjects were not randomized due to administrative reason by sponsor (20), subject no longer met study criteria (13), lost to follow-up (1), subject withdrew consent (1), and other reason (1).

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, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Peginterferon Lambda-1a + Ribavirin

Arm description:

Peginterferon Lambda-1a 180 µg solution for subcutaneous (sc) injection once weekly and Ribavirin 1000 or 1200 mg based on weight tablet by mouth twice daily for 48 weeks

Arm type	Experimental
Investigational medicinal product name	Ribavarin
Investigational medicinal product code	
Other name	Ribasphere; RBV
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

oral tablets administered twice a day for a total daily dose of 1000-1200 mg, for a maximum of 48 weeks.

Investigational medicinal product name	Peginterferon Lambda-1a
Investigational medicinal product code	
Other name	Lambda, BMS-914143
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

180 microgram subcutaneous (SC) injection once weekly

Arm title	Peginterferon alfa-2a + Ribavirin

Arm description:

Peginterferon alfa-2a 180 µg solution for subcutaneous (sc) injection once weekly and Ribavirin 1000 or 1200 mg based on weight tablet by mouth twice daily for 48 weeks

Arm type	Active comparator
Investigational medicinal product name	Peginterferon alfa-2a
Investigational medicinal product code	
Other name	Alfa-2a
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

180 microgram SC injection once weekly, for a maximum of 48 weeks

Number of subjects in period 1	Peginterferon Lambda-1a + Ribavirin	Peginterferon alfa-2a + Ribavirin
Started	26	13
Completed	20	7
Not completed	6	6
Adverse event, non-fatal	3	3
Lack of efficacy	3	3

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, Carer

Arms

Are arms mutually exclusive?	No
Arm title	Peginterferon Lambda-1a + Ribavirin

Arm description:

Peginterferon Lambda-1a 180 µg solution for subcutaneous (sc) injection once weekly and Ribavirin 1000 or 1200 mg based on weight tablet by mouth twice daily for 48 weeks

Arm type	Experimental
Investigational medicinal product name	Ribavarin
Investigational medicinal product code	
Other name	Ribasphere; RBV
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

oral tablets administered twice a day for a total daily dose of 1000-1200 mg, for a maximum of 48 weeks.

Investigational medicinal product name	Peginterferon Lambda-1a
Investigational medicinal product code	
Other name	Lambda, BMS-914143
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

180 microgram subcutaneous (SC) injection once weekly

Arm title	Peginterferon alfa-2a + Ribavirin

Arm description:

Peginterferon alfa-2a 180 µg solution for subcutaneous (sc) injection once weekly and Ribavirin 1000 or 1200 mg based on weight tablet by mouth twice daily for 48 weeks

Arm type	Active comparator

Investigational medicinal product name	Peginterferon alfa-2a
Investigational medicinal product code	
Other name	Alfa-2a
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

180 microgram SC injection once weekly, for a maximum of 48 weeks

Number of subjects in period 2	Peginterferon Lambda-1a + Ribavirin	Peginterferon alfa-2a + Ribavirin
Started	20	10
Completed	18	9
Not completed	2	1
Consent withdrawn by subject	1	1
not present in CSR Final	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Peginterferon Lambda-1a + Ribavirin
Reporting group description:	
Peginterferon Lambda-1a 180 µg solution for subcutaneous (sc) injection once weekly and Ribavirin 1000 or 1200 mg based on weight tablet by mouth twice daily for 48 weeks	
Reporting group title	Peginterferon alfa-2a + Ribavirin
Reporting group description:	
Peginterferon alfa-2a 180 µg solution for subcutaneous (sc) injection once weekly and Ribavirin 1000 or 1200 mg based on weight tablet by mouth twice daily for 48 weeks	

Reporting group values	Peginterferon Lambda-1a + Ribavirin	Peginterferon alfa-2a + Ribavirin	Total
Number of subjects	26	13	39
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	25	11	36
From 65-84 years	1	2	3
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	44.8	49.6	
standard deviation	± 10.98	± 12.31	-
Gender categorical Units: Subjects			
Female	17	1	18
Male	9	12	21

End points

End points reporting groups

Reporting group title	Peginterferon Lambda-1a + Ribavirin
Reporting group description:	
Peginterferon Lambda-1a 180 µg solution for subcutaneous (sc) injection once weekly and Ribavirin 1000 or 1200 mg based on weight tablet by mouth twice daily for 48 weeks	
Reporting group title	Peginterferon alfa-2a + Ribavirin
Reporting group description:	
Peginterferon alfa-2a 180 µg solution for subcutaneous (sc) injection once weekly and Ribavirin 1000 or 1200 mg based on weight tablet by mouth twice daily for 48 weeks	
Reporting group title	Peginterferon Lambda-1a + Ribavirin
Reporting group description:	
Peginterferon Lambda-1a 180 µg solution for subcutaneous (sc) injection once weekly and Ribavirin 1000 or 1200 mg based on weight tablet by mouth twice daily for 48 weeks	
Reporting group title	Peginterferon alfa-2a + Ribavirin
Reporting group description:	
Peginterferon alfa-2a 180 µg solution for subcutaneous (sc) injection once weekly and Ribavirin 1000 or 1200 mg based on weight tablet by mouth twice daily for 48 weeks	

Primary: Percentage of subjects who develop treatment emergent cytopenic abnormalities (anemia as defined by Hb < 10 g/dL, and/or neutropenia as defined by ANC < 750 mm3 and/or thrombocytopenia as defined by platelets < 50,000 mm3) in treatment-naive subjects

End point title	Percentage of subjects who develop treatment emergent cytopenic abnormalities (anemia as defined by Hb < 10 g/dL, and/or neutropenia as defined by ANC < 750 mm3 and/or thrombocytopenia as defined by platelets < 50,000 mm3) in treatment-naive subjects[1]

End point description:

Subjects in treatment with GT-1 chronic HCV (hepatitis C virus) infection the display cytopenic abnormalities (anemia is defined by Hb < 100 g/L, neutropenia as defined by ANC < 0.75 X 10*9 C/L and thrombocytopenia as defined by platelets < 50 X 10*9 C/L).

Subjects in treatment with GT-1 chronic HCV (hepatitis C virus) infection

*ANC - Absolute Neutrophil Count *Hb - Hemoglobin

End point type	Primary

End point timeframe:

Up to 48 weeks of treatment

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 summary statistics were planned for this endpoint.

End point values	Peginterferon Lambda-1a + Ribavirin	Peginterferon alfa-2a + Ribavirin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	13		
Units: percentage				
number (not applicable)				
Anemia	0	38.5		
Neutropenia	3.8	38.5		

Thrombocytopenia	0	7.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with Rapid Virologic Response (RVR) (HCV RNA not detected)

End point title	Percentage of subjects with Rapid Virologic Response (RVR) (HCV RNA not detected)[2]

End point description:

virologic responses for HCV RNA assessments

End point type	Secondary

End point timeframe:

On treatment Week 4 (of an up to 48-week treatment period)

Notes:

[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: Only these measurements were made for this endpoint.

End point values	Peginterferon Lambda-1a + Ribavirin			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: percentage				
number (not applicable)	23.1			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with on-treatment Serious Adverse Events (SAEs) through end of treatment

End point title	Percentage of subjects with on-treatment Serious Adverse Events (SAEs) through end of treatment[3]

End point description:

End point type	Secondary

End point timeframe:

Up to 48 weeks of treatment

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: Only these measurements were made for this endpoint.

End point values	Peginterferon Lambda-1a + Ribavirin			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: percentage				
number (not applicable)	11.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with dose reductions through end of treatment with Lambda (peginterferon lambda-1a)

End point title	Percentage of subjects with dose reductions through end of treatment with Lambda (peginterferon lambda-1a)

End point description:

The proportion of subjects who required one or more dose reductions during treatment with Lambda

End point type	Secondary

End point timeframe:

Up to 48 weeks of treatment

End point values	Peginterferon Lambda-1a + Ribavirin	Peginterferon alfa-2a + Ribavirin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	13		
Units: percentage				
number (not applicable)				
Hematologic Toxicity	0	0		
Non-hematologic Toxicity	0	0		
Elevated Liver Function Tests	11.5	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with dose reductions through end of treatment with Alfa (peginterferon alfa-2a)

End point title	Percentage of subjects with dose reductions through end of treatment with Alfa (peginterferon alfa-2a)

End point description:

The proportion of subjects who required one or more dose reductions during treatment with Alfa

End point type	Secondary

End point timeframe:

Up to 48 weeks of treatment

End point values	Peginterferon Lambda-1a + Ribavirin	Peginterferon alfa-2a + Ribavirin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	13		
Units: percentage				
number (not applicable)				
Hematologic Toxicity	0	46.2		
Non-hematologic Toxicity	0	46.2		
Elevated Liver Function Tests	0	7.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with dose reductions through end of treatment with Ribavirin

End point title	Percentage of subjects with dose reductions through end of treatment with Ribavirin
End point description:	
The proportion of subjects who required one or more dose reductions during treatment with Ribavirin	
End point type	Secondary
End point timeframe:	
up to 48 weeks of treatment	

End point values	Peginterferon Lambda-1a + Ribavirin	Peginterferon alfa-2a + Ribavirin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	13		
Units: percentage				
number (not applicable)				
Hematologic Toxicity	0	30.8		
Non-Hematologic Toxicity	0	7.7		
Elevated Liver Function Tests	3.8	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with on-treatment Interferon (IFN)-associated symptoms as determined by adverse event reporting

End point title	Percentage of subjects with on-treatment Interferon (IFN)-associated symptoms as determined by adverse event reporting

End point description:

On-treatment IFN-associated symptoms are: • Musculoskeletal symptoms (as defined by arthralgia or myalgia or back pain) • Neurological symptoms (headache or dizziness) • Psychiatric symptoms (depression or irritability or insomnia) • General Disorders including: Constitutional symptoms (fatigue or asthenia) • Flu-like symptoms (as defined by pyrexia or chills or pain)

End point type	Secondary

End point timeframe:

Up to 48 weeks of treatment

End point values	Peginterferon Lambda-1a + Ribavirin	Peginterferon alfa-2a + Ribavirin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	13		
Units: percentage				
number (not applicable)				
General Disorders (Symptoms)	46.2	46.2		
Musculoskeletal Symptoms	11.5	30.8		
Neurological (Nervous System) Symptoms	23.1	46.2		
Psychiatric Symptoms	46.2	15.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects who discontinue due to Adverse Events (AEs) through end of treatment

End point title	Percentage of subjects who discontinue due to Adverse Events (AEs) through end of treatment

End point description:

Subjects who did not complete full planned treatment duration

End point type	Secondary

End point timeframe:

Up to 48 weeks of treatment

End point values	Peginterferon Lambda-1a + Ribavirin	Peginterferon alfa-2a + Ribavirin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	13		
Units: percentage				
number (not applicable)	23.1	46.2		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From initiation of study drug to 30 days following discontinuation of drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Peginterferon Lambda-1a + Ribavirin

Reporting group description:

Peginterferon Lambda-1a 180 µg solution for subcutaneous (sc) injection once weekly and Ribavirin 1000 or 1200 mg based on weight tablet by mouth twice daily for 48 weeks

Reporting group title	Peginterferon alfa-2a + Ribavirin

Reporting group description:

Peginterferon alfa-2a 180 µg solution for subcutaneous (sc) injection once weekly and Ribavirin 1000 or 1200 mg based on weight tablet by mouth twice daily for 48 weeks

Serious adverse events	Peginterferon Lambda-1a + Ribavirin	Peginterferon alfa-2a + Ribavirin	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 26 (11.54%)	0 / 13 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Papillary Thyroid Cancer			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatitis Acute			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Infective chondritis			
alternative dictionary used:			

MedDRA 17.0			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Peginterferon Lambda-1a + Ribavirin	Peginterferon alfa-2a + Ribavirin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 26 (88.46%)	11 / 13 (84.62%)	
General disorders and administration site conditions			
Fatigue			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	5 / 26 (19.23%)	2 / 13 (15.38%)	
occurrences (all)	5	2	
Injection Site Rash			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	3 / 26 (11.54%)	0 / 13 (0.00%)	
occurrences (all)	3	0	
Influenza Like Illness			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 26 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Pyrexia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 26 (3.85%)	2 / 13 (15.38%)	
occurrences (all)	1	2	
Asthenia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 26 (0.00%)	3 / 13 (23.08%)	
occurrences (all)	0	3	
Chest Pain			
alternative dictionary used:			

MedDRA 17.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Fat Tissue Increased			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 26 (7.69%)	2 / 13 (15.38%)	
occurrences (all)	2	2	
Oropharyngeal Pain			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 26 (7.69%)	1 / 13 (7.69%)	
occurrences (all)	2	1	
Dyspnoea Exertional			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Productive Cough			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Pulmonary Mass			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Psychiatric disorders			
Insomnia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	10 / 26 (38.46%)	0 / 13 (0.00%)	
occurrences (all)	10	0	
Depression			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	3 / 26 (11.54%)	2 / 13 (15.38%)	
occurrences (all)	3	2	
Investigations			
Aspartate Aminotransferase Increased			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 26 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Alanine Aminotransferase Increased			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 26 (7.69%)	1 / 13 (7.69%)	
occurrences (all)	2	1	
Haemoglobin Decreased			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 26 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Neutrophil Count Decreased			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Platelet Count Decreased			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Weight Decreased			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
White Blood Cell Count Decreased			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Ligament Injury			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Cardiac disorders			
Palpitations			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 26 (3.85%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Nervous system disorders			
Headache			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	6 / 26 (23.08%)	3 / 13 (23.08%)	
occurrences (all)	6	3	
Paraesthesia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 26 (3.85%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Dizziness			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 26 (0.00%)	4 / 13 (30.77%)	
occurrences (all)	0	4	
Disturbance in Attention			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Thrombocytopenia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 26 (3.85%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Neutropenia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 26 (0.00%)	5 / 13 (38.46%)	
occurrences (all)	0	5	
Leukopenia			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Anaemia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 26 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Lymphadenpathy			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Eye disorders			
Ocular Hyperaemia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Dyspepsia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	5 / 26 (19.23%)	1 / 13 (7.69%)	
occurrences (all)	5	1	
Nausea			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	4 / 26 (15.38%)	4 / 13 (30.77%)	
occurrences (all)	4	4	
Diarrhoea			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 26 (7.69%)	2 / 13 (15.38%)	
occurrences (all)	2	2	
Abdominal Pain Upper			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 26 (3.85%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Dry Mouth			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	1 / 26 (3.85%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Toothache			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Hyperbilirubinaemia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 26 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Jaundice			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 26 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Hypertranaminasaemia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Pruritus			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	6 / 26 (23.08%)	2 / 13 (15.38%)	
occurrences (all)	6	2	
Rash			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	3 / 26 (11.54%)	2 / 13 (15.38%)	
occurrences (all)	3	2	
Alopecia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 26 (3.85%)	3 / 13 (23.08%)	
occurrences (all)	1	3	
Dermatitis			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	1 / 26 (3.85%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Dry Skin			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 26 (3.85%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Dermatitis Contact			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 26 (3.85%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Rash Erythematous			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Rash Generalised			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Myalgia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 26 (7.69%)	2 / 13 (15.38%)	
occurrences (all)	2	2	
Back Pain			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 26 (3.85%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Intervertebral Disc Protrusion			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 26 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Arthralgia			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Pain In Extremity			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Infections and infestations			
Upper Respiratory Tract Infection			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 26 (3.85%)	2 / 13 (15.38%)	
occurrences (all)	1	2	
Nasopharyngitis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 26 (3.85%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Gastroenteritis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Oral Herpes			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Otitis Media Acute			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased Appetite			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 26 (7.69%)	4 / 13 (30.77%)	
occurrences (all)	2	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 July 2013	The amendment is intended to exclude cirrhotics patients for enrollment in this study based on recent safety updates from patients who received Lambda, to incorporate updates and clarifications to study procedures and typo corrections and to incorporate some administrative changes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported