Clinical trial results:
A Long-Term Follow-Up Study of Subjects Who Participated in a Clinical Trial in which Peginterferon Lambda-1a (BMS-914143) was Administered for the Treatment of Chronic Hepatitis C

Summary

EudraCT number	2011-005293-31
Trial protocol	DE AT ES PL IT GR FI BE NL
Global end of trial date	11 November 2014

Results information

Result version number	v1 (current)
This version publication date	26 May 2016
First version publication date	26 May 2016

Trial information

Trial identification

Sponsor protocol code	AI452-016

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01525810
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	11 November 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 November 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to determine the durability of virologic response in subjects treated in a previous study with Lambda with or without Ribavirin and/or direct acting antiviral agents, who have Hepatitis C virus RNA less than the limit of quantitation of the assay at the completion of the required post-treatment follow-up in the previous (parent) study.

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 March 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 5
Country: Number of subjects enrolled	Australia: 35
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	Korea, Republic of: 8
Country: Number of subjects enrolled	Mexico: 7
Country: Number of subjects enrolled	New Zealand: 3
Country: Number of subjects enrolled	Romania: 20
Country: Number of subjects enrolled	Russian Federation: 11
Country: Number of subjects enrolled	United States: 44
Country: Number of subjects enrolled	Netherlands: 3
Country: Number of subjects enrolled	Poland: 18
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Finland: 8
Country: Number of subjects enrolled	France: 22

Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Greece: 3
Country: Number of subjects enrolled	Italy: 19
Worldwide total number of subjects	235
EEA total number of subjects	117

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)	222
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 64 sites in 20 countries.

Pre-assignment

Screening details:

A total of 235 eligible subjects were enrolled from 5 different studies AI452004 (526H04), AI452008, AI452017, AI452020, and AI452021. The analysis was focused on the 200 subjects who received Lambda in the parent study.

Period 1

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

Arms

Arm title	Lambda-treated

Arm description:

Subjects with Hepatitis C virus RNA <lower limit of quantitation, target detected or target not detected, who were previously treated with peginterferon lambda-1a in combination with or without ribavirin and/or other direct acting antiviral agents within 6 months after completion of follow-up in the parent study.

Arm type	Observational
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:

Subjects were previously treated with Peginterferon Lambda-1a.

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

Dosage and administration details:

Subjects were previously treated with Peginterferon Lambda-1a in combination with or without ribavirin.

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

Dosage and administration details:

Subjects were previously treated with Peginterferon Lambda-1a in combination with daclatasvir with or without ribavirin.

Number of subjects in period 1[1]	Lambda-treated
Started	200
Completed	0
Not completed	200
Consent withdrawn by subject	5
Other	4
Lost to follow-up	8
Administrative reason by sponsor	183

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 235 eligible subjects who were enrolled, the analysis was focused on the 200 subjects who received Lambda in the parent study.

Baseline characteristics

Reporting groups	
Reporting group title	Lambda-treated
Reporting group description:	
Subjects with Hepatitis C virus RNA <lower limit of quantitation, target detected or target not detected, who were previously treated with peginterferon lambda-1a in combination with or without ribavirin and/or other direct acting antiviral agents within 6 months after completion of follow-up in the parent study.	

Reporting group values	Lambda-treated	Total	
Number of subjects	200	200	
Age categorical Units: Subjects			
<65 years	191	191	
>=65 years	9	9	
Age continuous Units: years			
arithmetic mean	46.1		
full range (min-max)	20 to 75	-	
Gender categorical Units: Subjects			
Female	89	89	
Male	111	111	

End points

End points reporting groups

Reporting group title	Lambda-treated

Reporting group description:

Subjects with Hepatitis C virus RNA <lower limit of quantitation, target detected or target not detected, who were previously treated with peginterferon lambda-1a in combination with or without ribavirin and/or other direct acting antiviral agents within 6 months after completion of follow-up in the parent study.

Primary: Percentage of Hepatitis C Virus (HCV) subjects With Durable Virologic Response

End point title	Percentage of Hepatitis C Virus (HCV) subjects With Durable Virologic Response[1]

End point description:

Durability of virologic response was defined as the time to loss of virologic response assessed by HCV RNA levels in subjects treated in a previous study with BMS-914143 who had HCV RNA <lower limit of quantitation (LLOQ) (target detected or target not detected) at the completion of the required post-treatment follow-up in the previous (parent) study. The analysis was performed in all the subjects with HCV RNA <LLOQ, who were previously treated with peginterferon lambda-1a in combination with or without ribavirin and/or other direct acting antiviral agents within 6 months after completion of follow-up in the parent study.

End point type	Primary

End point timeframe:

Day 1 and at follow-up Week 24, 48, 72, and 96 (early termination of study)

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.

End point values	Lambda-treated			
Subject group type	Reporting group			
Number of subjects analysed	200			
Units: Percentage of subject				
number (not applicable)	0.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Long-Term Progression of Liver Disease

End point title	Number of Subjects With Long-Term Progression of Liver Disease

End point description:

Long-term progression of liver disease was measured by laboratory indicators of hepatic status and function, all-cause mortality and liver related mortality in subjects previously treated with BMS-914143 who have Hepatitis C virus (HCV) RNA <lower limit of quantitation (LLOQ) (target detected or target not detected) at the completion of the required post-treatment follow-up in the parent study. The analysis was performed in all the subjects with HCV RNA < LLOQ, who were previously treated with peginterferon lambda-1a in combination with or without ribavirin and/or other direct acting antiviral

agents within 6 months after completion of follow-up in the parent study.

End point type	Secondary

End point timeframe:

Day 1 and at follow-up Week 24, 48, 72, and 96 (early termination of study)

End point values	Lambda-treated			
Subject group type	Reporting group			
Number of subjects analysed	200			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Persistence of Anti-Lambda Antibodies (ADA) in Subjects Who Are Positive For Anti-Lambda Antibodies at End of Treatment in The Parent Study

End point title	Duration of Persistence of Anti-Lambda Antibodies (ADA) in Subjects Who Are Positive For Anti-Lambda Antibodies at End of Treatment in The Parent Study

End point description:

The duration of persistence of ADA in eligible Lambda-treated subjects who were positive at end of treatment (EOT) in the parent study was summarized using a Kaplan-Meier life table. For subjects who had ADA-positive samples and then became ADA-negative, the duration of persistence of ADA was measured from EOT in the parent study to the time of the first confirmed negative sample. For subjects who had ADA-positive samples in the parent study and did not become ADA-negative during follow-up in AI452016 study, the duration of persistence of ADA was measured from EOT in the parent study to the time of the last positive anti-Lambda antibody sample. The analysis was performed in all the subjects who were positive for anti-Lambda antibodies at the end of treatment in the parent study. Here, '99999' represents not estimable data.

End point type	Secondary

End point timeframe:

Day 1 and at follow-up Week 24, 48, 72, and 96 (early termination of study)

End point values	Lambda-treated			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: Weeks				
number (not applicable)				

Notes:

[2] - The study was prematurely terminated.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Day 1 and at follow-up Week 24, 48, 72, and 96 (early termination of study)

Assessment type	Systematic

Dictionary used

Dictionary name	NIL
Dictionary version	0.0

Reporting groups

Reporting group title	Lambda-treated

Reporting group description:

Subjects with Hepatitis C virus RNA <lower limit of quantitation (target detected or target not detected) who were previously treated with peginterferon lambda-1a in combination with or without RBV and/or other direct acting antiviral agents within 6 months after completion of follow-up in the parent study.

Serious adverse events	Lambda-treated		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 200 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	Lambda-treated		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 200 (0.00%)		

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: The study was prematurely terminated and safety data was collected if it was considered related to peginterferon lambda-1a.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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 due to the availability of effective all-oral hepatitis C virus (HCV) treatment regimens which had changed the clinical landscape significantly, and reduced the unmet medical need in HCV.

Notes: