Clinical trial results:
LIRA-B - Dose-Ranging Study to Evaluate the Safety, Efficacy and Pharmacokinetics of Pegylated Interferon Lambda (BMS-914143) Monotherapy in Interferon-Naive Patients with Chronic Hepatitis B Virus Infection who are HBeAg-positive.

Summary

EudraCT number	2010-020387-38
Trial protocol	DE IT NL
Global end of trial date	13 December 2013

Results information

Result version number	v1 (current)
This version publication date	31 July 2016
First version publication date	31 July 2016

Trial information

Trial identification

Sponsor protocol code	AI452-005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01204762
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	13 December 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 December 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objectives of the trial were to evaluate the safety and tolerability of Pegylated Interferon Lambda as measured by the frequency of serious adverse events and discontinuations due to adverse events and to assess the hepatitis B e antigen seroconversion rate at 24 weeks (Week 72) off treatment.

Protection of trial subjects:

The study was conducted 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	15 November 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	30 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	France: 14
Country: Number of subjects enrolled	Germany: 17
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	Australia: 20
Country: Number of subjects enrolled	Canada: 35
Country: Number of subjects enrolled	Hong Kong: 35
Country: Number of subjects enrolled	Korea, Republic of: 62
Country: Number of subjects enrolled	Singapore: 14
Country: Number of subjects enrolled	Taiwan: 65
Country: Number of subjects enrolled	United States: 57
Worldwide total number of subjects	333
EEA total number of subjects	45

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)	332
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled at 52 sites in 11 countries.

Pre-assignment

Screening details:

A total of 333 subjects were enrolled in this study. Part A: Out of 298 subjects enrolled, 177 subjects were randomised and 176 were treated. Reasons for 121 subjects not randomised were: subject withdrew consent (7), subjects no longer met study criteria (107), and other reasons (7). Part B: A total of 21 subjects were treated.

Period 1

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

Blinding implementation details:

Part B of the study was open-label.

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A: Peginterferon Lambda 240 µg

Arm description:

Subjects were administered Peginterferon Lambda 240 µg via subcutaneous injection, once weekly, for a planned duration of 48 weeks. All 13 subjects who were initially assigned to 240 µg Lambda subsequently had their dose dropped to 180 µg following a decision by the sponsor to discontinue development of this Lambda dose due to safety reasons.

Arm type	Experimental
Investigational medicinal product name	Pegylated Interferon Lambda
Investigational medicinal product code	BMS-914143
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were administered Peginterferon Lambda 240 µg via subcutaneous injection, once weekly, for a planned duration of 48 weeks. All 13 subjects who were initially assigned to 240 µg Lambda subsequently had their dose dropped to 180 µg following a decision by the sponsor to discontinue development of this Lambda dose due to safety reasons.

Arm title	Part A: Peginterferon Lambda 180 µg

Arm description:

Subjects were administered Peginterferon Lambda 180 µg via subcutaneous injection, once weekly, for a planned duration of 48 weeks.

Arm type	Experimental
Investigational medicinal product name	Pegylated Interferon Lambda
Investigational medicinal product code	BMS-914143
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were administered Pegylated Interferon Lambda 180 µg via subcutaneous injection, once weekly, for a planned duration of 48 weeks.

Arm title	Part A: Peginterferon alfa-2a 180 µg

Arm description:

Subjects were administered Peginterferon alfa-2a 180 µg via subcutaneous injection, once weekly, for a planned duration of 48 weeks.

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

Dosage and administration details:

Subjects were administered Peginterferon alfa- 2a 180 µg via subcutaneous injection, once weekly, for a planned duration of 48 weeks.

Arm title	Part B: Peginterferon Lambda + Entecavir

Arm description:

Subjects with hepatitis E antigen-positive (HBeAg-positive) chronic hepatitis B virus (HBV) infection received HBV treatment for a planned duration of 60 weeks: Entecavir 0.5 mg tablets administered orally, once daily, for 12 weeks followed by Peginterferon Lambda 180 µg, administered subcutaneously, once weekly, along with Entecavir 0.5 mg, tablets, administered orally, once daily for 48 weeks.

Arm type	Experimental
Investigational medicinal product name	Pegylated Interferon Lambda
Investigational medicinal product code	BMS-914143
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were administered Pegylated Interferon Lambda 180 µg via subcutaneous injection, once weekly, for a planned duration of 48 weeks.

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

Dosage and administration details:

Subjects were administered Entecavir 0.5 mg film-coated tablets, orally, once daily for 60 weeks (12 weeks as monotherapy and 48 weeks in combination with peginterferon lambda).

Number of subjects in period 1[1]	Part A: Peginterferon Lambda 240 µg	Part A: Peginterferon Lambda 180 µg	Part A: Peginterferon alfa-2a 180 µg
Started	13	80	83
Completed	9	74	68
Not completed	4	6	15
Consent withdrawn by subject	-	-	3
Adverse event, non-fatal	3	6	8
Subject request to discontinue study treatment	1	-	1
Pregnancy	-	-	-
Other reasons	-	-	-

Lost to follow-up	-	-	1
Lack of efficacy	-	-	2
Administrative reason by sponsor	-	-	-

Number of subjects in period 1[1]	Part B: Peginterferon Lambda + Entecavir
Started	21
Completed	6
Not completed	15
Consent withdrawn by subject	-
Adverse event, non-fatal	-
Subject request to discontinue study treatment	-
Pregnancy	1
Other reasons	3
Lost to follow-up	1
Lack of efficacy	-
Administrative reason by sponsor	10

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: Part A: Out of 298 subjects enrolled, 177 subjects were randomised and 176 were treated. Part B: A total of 21 subjects were treated.

Period 2

Period 2 title	Follow-up Period (24 weeks)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A: Peginterferon Lambda 240 µg

Arm description:

Subjects were followed up for 24 weeks after receiving Peginterferon Lambda 240 µg via subcutaneous injection, once weekly, for a planned duration of 48 weeks. All subjects who were initially assigned to 240 µg Lambda subsequently had their dose dropped to 180 µg.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Part A: Peginterferon Lambda 180 µg

Arm description:

Subjects were followed up for 24 weeks after receiving Peginterferon Lambda 180 µg via subcutaneous injection, once weekly, for a planned duration of 48 weeks.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Part A: Peginterferon alfa-2a 180 µg

Arm description:

Subjects were followed up for 24 weeks after receiving Peginterferon alfa-2a 180 µg via subcutaneous injection, once weekly, for a planned duration of 48 weeks.

Arm type	No intervention

No investigational medicinal product assigned in this arm	
Arm title	Part B: Peginterferon Lambda + Entecavir

Arm description:

Subjects with hepatitis E antigen-positive (HBeAg-positive) chronic hepatitis B virus (HBV) infection were to be followed up for 24 weeks after receiving HBV treatment for a planned duration of 60 weeks: Entecavir 0.5 mg tablets administered orally, once daily for 12 weeks followed by Peginterferon Lambda 180 µg, administered subcutaneously, once weekly along with Entecavir 0.5 mg, tablets, administered orally, once daily for 48 weeks

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

Number of subjects in period 2	Part A: Peginterferon Lambda 240 µg	Part A: Peginterferon Lambda 180 µg	Part A: Peginterferon alfa-2a 180 µg
Started	9	74	68
Completed	11	70	72
Not completed	1	8	6
Consent withdrawn by subject	1	3	4
Other reason	-	1	-
Lost to follow-up	-	2	1
Subject no longer meets study criteria	-	1	1
Lack of efficacy	-	1	-
Administrative reason by sponsor	-	-	-
Joined	3	4	10
Re-joined for follow-up	3	4	10

Number of subjects in period 2	Part B: Peginterferon Lambda + Entecavir
Started	6
Completed	0
Not completed	9
Consent withdrawn by subject	-
Other reason	-
Lost to follow-up	-
Subject no longer meets study criteria	-
Lack of efficacy	-
Administrative reason by sponsor	9
Joined	3
Re-joined for follow-up	3

Period 3

Period 3 title	Long-Term Follow-up
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A: Peginterferon Lambda 240 µg

Arm description:

Subjects were to be followed up for 36 months after completion of 24 weeks post follow-up after receiving Peginterferon Lambda 240 µg, subcutaneously, once weekly for a planned duration of 48 weeks during the treatment period. All 13 subjects who were initially assigned to 240 µg Lambda subsequently had their dose dropped to 180 µg following a decision by the sponsor to discontinue development of this Lambda dose due to safety reasons.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Part A: Peginterferon Lambda 180 µg

Arm description:

Subjects were to be followed up for 36 months after completion of 24 weeks post follow-up after receiving Peginterferon Lambda 180 µg, subcutaneously, once weekly for a planned duration of 48 weeks during the treatment period.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Part A: Peginterferon alfa-2a 180 µg

Arm description:

Subjects were to be followed up for 36 months after completion of 24 weeks post follow-up after receiving Peginterferon alfa-2a 180 µg, subcutaneously, once weekly for a planned duration of 48 weeks during the treatment period.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 3[2]	Part A: Peginterferon Lambda 240 µg	Part A: Peginterferon Lambda 180 µg	Part A: Peginterferon alfa-2a 180 µg
Started	3	28	39
Completed	0	2	3
Not completed	3	26	36
Consent withdrawn by subject	-	3	-
Other reasons	3	21	35
Lost to follow-up	-	2	1

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Out of 153 subjects who completed the 24 weeks follow-up period, only 70 subjects

entered the long-term follow-up period.

Baseline characteristics

Reporting groups	
Reporting group title	Part A: Peginterferon Lambda 240 µg
Reporting group description:	
Subjects were administered Peginterferon Lambda 240 µg via subcutaneous injection, once weekly, for a planned duration of 48 weeks. All 13 subjects who were initially assigned to 240 µg Lambda subsequently had their dose dropped to 180 µg following a decision by the sponsor to discontinue development of this Lambda dose due to safety reasons.	
Reporting group title	Part A: Peginterferon Lambda 180 µg
Reporting group description:	
Subjects were administered Peginterferon Lambda 180 µg via subcutaneous injection, once weekly, for a planned duration of 48 weeks.	
Reporting group title	Part A: Peginterferon alfa-2a 180 µg
Reporting group description:	
Subjects were administered Peginterferon alfa-2a 180 µg via subcutaneous injection, once weekly, for a planned duration of 48 weeks.	
Reporting group title	Part B: Peginterferon Lambda + Entecavir
Reporting group description:	
Subjects with hepatitis E antigen-positive (HBeAg-positive) chronic hepatitis B virus (HBV) infection received HBV treatment for a planned duration of 60 weeks: Entecavir 0.5 mg tablets administered orally, once daily, for 12 weeks followed by Peginterferon Lambda 180 µg, administered subcutaneously, once weekly, along with Entecavir 0.5 mg, tablets, administered orally, once daily for 48 weeks.	

Reporting group values	Part A: Peginterferon Lambda 240 µg	Part A: Peginterferon Lambda 180 µg	Part A: Peginterferon alfa-2a 180 µg
Number of subjects	13	80	83
Age categorical Units: Subjects			
<21 years	0	0	1
21 - <65 years	13	80	82
>=65 years	0	0	0
Age continuous Units: years			
arithmetic mean	33.1	36.5	34.9
standard deviation	± 7.17	± 10.19	± 8.9
Gender categorical Units: Subjects			
Female	1	21	20
Male	12	59	63

Reporting group values	Part B: Peginterferon Lambda + Entecavir	Total	
Number of subjects	21	197	
Age categorical Units: Subjects			
<21 years	0	1	
21 - <65 years	21	196	
>=65 years	0	0	

Age continuous Units: years			
arithmetic mean	34		
standard deviation	± 7.86	-	
Gender categorical Units: Subjects			
Female	6	48	
Male	15	149	

End points

End points reporting groups

Reporting group title	Part A: Peginterferon Lambda 240 µg

Reporting group description:

Subjects were administered Peginterferon Lambda 240 µg via subcutaneous injection, once weekly, for a planned duration of 48 weeks. All 13 subjects who were initially assigned to 240 µg Lambda subsequently had their dose dropped to 180 µg following a decision by the sponsor to discontinue development of this Lambda dose due to safety reasons.

Reporting group title	Part A: Peginterferon Lambda 180 µg

Reporting group description:

Subjects were administered Peginterferon Lambda 180 µg via subcutaneous injection, once weekly, for a planned duration of 48 weeks.

Reporting group title	Part A: Peginterferon alfa-2a 180 µg

Reporting group description:

Subjects were administered Peginterferon alfa-2a 180 µg via subcutaneous injection, once weekly, for a planned duration of 48 weeks.

Reporting group title	Part B: Peginterferon Lambda + Entecavir

Reporting group description:

Subjects with hepatitis E antigen-positive (HBeAg-positive) chronic hepatitis B virus (HBV) infection received HBV treatment for a planned duration of 60 weeks: Entecavir 0.5 mg tablets administered orally, once daily, for 12 weeks followed by Peginterferon Lambda 180 µg, administered subcutaneously, once weekly, along with Entecavir 0.5 mg, tablets, administered orally, once daily for 48 weeks.

Reporting group title	Part A: Peginterferon Lambda 240 µg

Reporting group description:

Subjects were followed up for 24 weeks after receiving Peginterferon Lambda 240 µg via subcutaneous injection, once weekly, for a planned duration of 48 weeks. All subjects who were initially assigned to 240 µg Lambda subsequently had their dose dropped to 180 µg.

Reporting group title	Part A: Peginterferon Lambda 180 µg

Reporting group description:

Subjects were followed up for 24 weeks after receiving Peginterferon Lambda 180 µg via subcutaneous injection, once weekly, for a planned duration of 48 weeks.

Reporting group title	Part A: Peginterferon alfa-2a 180 µg

Reporting group description:

Subjects were followed up for 24 weeks after receiving Peginterferon alfa-2a 180 µg via subcutaneous injection, once weekly, for a planned duration of 48 weeks.

Reporting group title	Part B: Peginterferon Lambda + Entecavir

Reporting group description:

Subjects with hepatitis E antigen-positive (HBeAg-positive) chronic hepatitis B virus (HBV) infection were to be followed up for 24 weeks after receiving HBV treatment for a planned duration of 60 weeks: Entecavir 0.5 mg tablets administered orally, once daily for 12 weeks followed by Peginterferon Lambda 180 µg, administered subcutaneously, once weekly along with Entecavir 0.5 mg, tablets, administered orally, once daily for 48 weeks

Reporting group title	Part A: Peginterferon Lambda 240 µg

Reporting group description:

Subjects were to be followed up for 36 months after completion of 24 weeks post follow-up after receiving Peginterferon Lambda 240 µg, subcutaneously, once weekly for a planned duration of 48 weeks during the treatment period. All 13 subjects who were initially assigned to 240 µg Lambda subsequently had their dose dropped to 180 µg following a decision by the sponsor to discontinue development of this Lambda dose due to safety reasons.

Reporting group title	Part A: Peginterferon Lambda 180 µg

Reporting group description:

Subjects were to be followed up for 36 months after completion of 24 weeks post follow-up after receiving Peginterferon Lambda 180 µg, subcutaneously, once weekly for a planned duration of 48 weeks during the treatment period.

Reporting group title	Part A: Peginterferon alfa-2a 180 µg

Reporting group description:

Subjects were to be followed up for 36 months after completion of 24 weeks post follow-up after receiving Peginterferon alfa-2a 180 µg, subcutaneously, once weekly for a planned duration of 48 weeks during the treatment period.

Primary: Percentage of Subjects Who Achieved Hepatitis B e Antigen (HBeAg) Seroconversion at Follow-up Week 24 - Part A

End point title	Percentage of Subjects Who Achieved Hepatitis B e Antigen (HBeAg) Seroconversion at Follow-up Week 24 - Part A[1]

End point description:

HBeAg seroconversion was defined as having a post-baseline negative serum HBeAg and simultaneous positive Hepatitis B e antibody (HBeAb) for subjects with positive serum HBeAg and negative HBeAb at screening. HBeAG levels were measured using commercially available qualitative HBeAg (qHBeAg) assays. The analysis was performed in all treated subjects using modified intent-to-treat algorithm (numerator is based on subjects meeting the response criteria and the denominator is based on all treated subjects (Non-completer = Failure).

End point type	Primary

End point timeframe:

Follow-up Week 24

Notes:

[1] - 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 only the specified arms.

End point values	Part A: Peginterferon Lambda 240 µg	Part A: Peginterferon Lambda 180 µg	Part A: Peginterferon alfa-2a 180 µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	80	83	
Units: Percentage of subjects				
number (confidence interval 80%)	7.7 (0 to 17.2)	13.8 (8.8 to 18.7)	30.1 (23.7 to 36.6)	

Statistical analyses

Statistical analysis title	HBeAG seroconversion rate
Comparison groups	Part A: Peginterferon Lambda 180 µg v Part A: Peginterferon alfa-2a 180 µg
Number of subjects included in analysis	163
Analysis specification	Pre-specified
Analysis type	other[2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportions
Point estimate	-0.1635
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-0.2425
upper limit	-0.0845

Notes:

[2] - A 2-stage testing procedure was planned. In the first stage, non-inferiority of Lambda to alfa would be tested. Provided non-inferiority was met, superiority of Lambda to alfa would be tested. Non-inferiority of Lambda to alfa was not met because the lower bound of the 80% confidence limit was < -15%, the pre-specified non-inferiority margin. Thus, superiority was not tested."

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

End point title	Number of Subjects With Serious Adverse Events (SAEs) and Discontinuation Due to Adverse Events (AEs)[3]

End point description:

AE=any new unfavorable symptom, sign, or disease or worsening of a preexisting condition that may not have a causal relationship with treatment. SAE=a medical event that at any dose results in death, persistent or significant disability/incapacity, or drug dependency/abuse; is life-threatening, an important medical event, or a congenital anomaly/birth defect; or requires or prolongs hospitalization. Analysis population included all treated subjects.

End point type	Primary

End point timeframe:

Day 1 to end of treatment plus 10 days

Notes:

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

End point values	Part A: Peginterferon Lambda 240 µg	Part A: Peginterferon Lambda 180 µg	Part A: Peginterferon alfa-2a 180 µg	Part B: Peginterferon Lambda + Entecavir
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	80	83	21
Units: Subjects				
SAEs	3	7	5	0
Discontinuation due to AEs	3	6	8	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Hepatitis B Virus (HBV) DNA <50 IU/mL - Part A

End point title	Percentage of Subjects With Hepatitis B Virus (HBV) DNA <50 IU/mL - Part A[4]

End point description:

HBV DNA was measured by polymerase chain reaction (PCR) using the Roche COBAS TaqMan - High Pure System (HPS) assay with lower limit of quantification (LOQ) = 29 IU/mL and limit of detection (LOD) = 10 IU/mL. The analysis was performed in all treated subjects using modified intent-to-treat (ITT) algorithm (numerator is based on subjects meeting the response criteria and the denominator is based on all treated subjects (Non-completer = Failure). Here, '99999' represents not estimable data for specified categories in respective arms.

End point type	Secondary

End point timeframe:

Weeks 12, 24, 48, 72, 96, 120, 144, 168, and 192

Notes:

[4] - 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 only the specified arms.

End point values	Part A: Peginterferon Lambda 240 µg	Part A: Peginterferon Lambda 180 µg	Part A: Peginterferon alfa-2a 180 µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	80	83	
Units: Percentage of subjects				
number (confidence interval 80%)				
Week 12	99999 (99999 to 99999)	5 (1.9 to 8.1)	0 (0 to 0)	
Week 24	7.7 (0 to 17.2)	10 (5.7 to 14.3)	1.2 (0 to 2.7)	
Week 48	0 (0 to 0)	13.8 (8.8 to 18.7)	10.8 (6.5 to 15.2)	
Week 72	0 (0 to 0)	6.3 (2.8 to 9.7)	1.2 (0 to 2.7)	
Week 96	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	
Week 120	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	
Week 144	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	
Week 168	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	
Week 192	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Log10 HBV DNA levels - Part A

End point title	Mean Change From Baseline in Log10 HBV DNA levels - Part

End point description:

HBV DNA was measured by PCR using the Roche COBAS TaqMan - HPS assay with LOQ = 29 IU/mL and LOD = 10 IU/mL. Values below LOQ were set to LOQ-1. HBV DNA levels were converted to the log10 scale. Analysis population included all treated subjects. Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms and '99999' represents not estimable data for specified categories in respective arms.

End point type	Secondary

End point timeframe:

Baseline and Weeks 2, 4, 8, 12, 16, 24, 48, 72, 96, 120, 144, 168, 192

Notes:

[5] - 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 only the specified arms.

End point values	Part A: Peginterferon Lambda 180 µg	Part A: Peginterferon alfa-2a 180 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	83		
Units: IU/mL				
arithmetic mean (standard error)				
Week 2 (n=75, 78)	-0.93 (± 0.0883)	-0.475 (± 0.0562)		
Week 4 (n=76, 81)	-1.515 (± 0.095)	-0.876 (± 0.0864)		
Week 8 (n=30, 35)	-2.288 (± 0.261)	-1.51 (± 0.2207)		
Week 12 (n=73, 75)	-2.602 (± 0.1808)	-1.778 (± 0.1743)		
Week 16 (n=72, 74)	-2.692 (± 0.2109)	-2.027 (± 0.1991)		
Week 24 (n=73, 72)	-2.782 (± 0.233)	-2.276 (± 0.2124)		
Week 48 (n=69, 65)	-2.667 (± 3.402)	-2.876 (± 3.469)		
Week 72 (n=55, 61)	-1.295 (± 3.856)	-2.093 (± 4.173)		
Week 96 (n=24, 32)	-2.571 (± 0.5387)	-2.412 (± 0.4353)		
Week 120 (n=0, 0)	99999 (± 99999)	99999 (± 99999)		
Week 144 (n=0, 0)	99999 (± 99999)	99999 (± 99999)		
Week 168 (n=0, 0)	99999 (± 99999)	99999 (± 99999)		
Week 192 (n=0, 0)	99999 (± 99999)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Alanine Aminotransferase (ALT) Normalization - Part A

End point title	Percentage of Subjects with Alanine Aminotransferase (ALT) Normalization - Part A[6]

End point description:

ALT normalization was defined as having ALT values <=1*Upper Limit of Normal (ULN) in subjects who have values >ULN at screening. The analysis was performed in all treated subjects using modified ITT algorithm (numerator is based on subjects meeting the response criteria and the denominator is based on all treated subjects (Non-completer = Failure). Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms and '99999' represents not estimable data for specified categories in respective arms.

End point type	Secondary

End point timeframe:

Weeks 24, 48, 72, 96, 120, 144, 168, and 192

Notes:

[6] - 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 only the specified arms.

End point values	Part A: Peginterferon Lambda 180 µg	Part A: Peginterferon alfa-2a 180 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	83		
Units: Percentage of subjects				
number (confidence interval 80%)				
Week 24 (n=80, 83)	23.8 (17.7 to 29.8)	33.7 (27.1 to 40.4)		
Week 48 (n=80, 83)	32.5 (25.8 to 39.2)	32.5 (25.9 to 39.1)		
Week 72 (n=80, 83)	43.8 (36.6 to 50.9)	51.8 (44.8 to 58.8)		
Week 96 (n=0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		
Week 120 (n=0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		
Week 144 (n=0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		
Week 168 (n=0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		
Week 192 (n=0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With HBeAg Loss - Part A

End point title	Percentage of Subjects With HBeAg Loss - Part A[7]

End point description:

HBeAg loss was defined as having negative post-baseline serum HBeAg for subjects with positive serum HBeAg at screening. HBeAG levels were measured using commercially available quantitative HBeAg (qHBeAg) assays. The analysis was performed in all treated subjects using modified ITT algorithm (numerator is based on subjects meeting the response criteria and the denominator is based on all treated subjects (Non-completer = Failure). Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms and '99999' represents not estimable data for specified categories in respective arms.

End point type	Secondary

End point timeframe:

Weeks 12, 24, 48, 72, 96, 120, 144, 168, and 192

Notes:

[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 only the specified arms.

End point values	Part A: Peginterferon Lambda 240 µg	Part A: Peginterferon Lambda 180 µg	Part A: Peginterferon alfa-2a 180 µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	80	83	
Units: Percentage of subjects				
number (confidence interval 80%)				
Week 12 (n=13, 80, 83)	99999 (99999 to 99999)	7.5 (3.7 to 11.3)	7.2 (3.6 to 10.9)	

Week 24 (n=13, 80, 83)	0 (0 to 0)	8.8 (4.7 to 12.8)	8.4 (4.5 to 12.3)	
Week 48 (n=13, 80, 83)	7.7 (0 to 17.2)	18.8 (13.2 to 24.3)	18.1 (12.7 to 23.5)	
Week 72 (n=13, 80, 83)	7.7 (0 to 17.2)	15 (9.9 to 20.1)	32.5 (25.9 to 39.1)	
Week 96 (n=0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	
Week 120 (n=0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	
Week 144 (n=0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	
Week 168 (n=0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	
Week 192 (n=0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With HBeAg Seroconversion - Part A

End point title	Percentage of Subjects With HBeAg Seroconversion - Part A[8]

End point description:

HBeAG seroconversion was defined as having a post-baseline negative serum HBeAg and simultaneous positive HBeAb for subjects with positive serum HBeAg and negative HBeAb at screening. HBeAG levels were measured using commercially available quantitative HBeAg (qHBeAg) assays (ARCHITECT [Abbott]). The analysis was performed in all treated subjects using modified ITT algorithm (numerator is based on subjects meeting the response criteria and the denominator is based on all treated subjects (Non-completer = Failure). Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms and '99999' represents not estimable data for specified categories in respective arms.

End point type	Secondary

End point timeframe:

Weeks 12, 24, 48, 72, 96, 120, 144, 168, and 192

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 only the specified arms.

End point values	Part A: Peginterferon Lambda 240 µg	Part A: Peginterferon Lambda 180 µg	Part A: Peginterferon alfa-2a 180 µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	80	83	
Units: Percentage of subjects				
number (confidence interval 80%)				
Week 12 (n=13, 80, 83)	99999 (99999 to 99999)	6.3 (2.8 to 9.7)	6 (2.7 to 9.4)	
Week 24 (n=13, 80, 83)	0 (0 to 0)	6.3 (2.8 to 9.7)	8.4 (4.5 to 12.3)	
Week 48 (n=13, 80, 83)	7.7 (0 to 17.2)	17.5 (12.1 to 22.9)	16.9 (11.6 to 22.1)	
Week 72 (n=13, 80, 83)	7.7 (0 to 17.2)	13.8 (8.8 to 18.7)	30.1 (23.7 to 36.6)	
Week 96 (n=0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	

Week 120 (n=0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	
Week 144 (n=0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	
Week 168 (n=0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	
Week 192 (n=0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Log10 Quantitative HBeAg - Part A

End point title	Mean Change From Baseline in Log10 Quantitative HBeAg - Part A[9]

End point description:

HBeAG levels were measured using commercially available quantitative HBeAg (qHBeAg) assays (ARCHITECT [Abbott]). The dynamic range of the qHBeAg assay is 0.22-56.70 Paul Erhlich Institute (PEI) U/mL and the assay is currently validated to dilute samples with a concentration of up to 567 PEI U/mL. Values below the lower LOQ were set to lower LOQ/2. Values above the upper LOQ were set to upper LOQ+1. qHBeAg values were converted to the log 10 scale. Analysis population included all treated subjects. Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms and '99999' represents not estimable data for specified categories in respective arms.

End point type	Secondary

End point timeframe:

Weeks 12, 24, 48, 72, 96, 120, 144, 168, and 192

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 only the specified arms.

End point values	Part A: Peginterferon Lambda 180 µg	Part A: Peginterferon alfa-2a 180 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	83		
Units: IU/mL				
arithmetic mean (standard error)				
Week 12 (n=71, 74)	-0.954 (± 0.107)	-0.719 (± 0.1114)		
Week 24 (n=71, 70)	-1.067 (± 0.1212)	-0.965 (± 0.1301)		
Week 48 (n=68, 62)	-1.191 (± 2.239)	-1.347 (± 1.974)		
Week 72 (n=51, 58)	-0.869 (± 0.2024)	-1.496 (± 0.2013)		
Week 96 (n=0, 0)	99999 (± 99999)	99999 (± 99999)		
Week 120 (n=0, 0)	99999 (± 99999)	99999 (± 99999)		
Week 144 (n=0, 0)	99999 (± 99999)	99999 (± 99999)		
Week 168 (n=0, 0)	99999 (± 99999)	99999 (± 99999)		

Week 192 (n=0, 0)	99999 (± 99999)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With SAEs, Discontinuations Due to AEs, AEs Leading to Dose Reduction, Grade 1 to 4 AEs, Grade 3 to 4 AEs, and Discontinuations Due to Treatment-Limiting Toxicity (TLT)-Treatment Period (Part A)

End point title	Number of Subjects With SAEs, Discontinuations Due to AEs, AEs Leading to Dose Reduction, Grade 1 to 4 AEs, Grade 3 to 4 AEs, and Discontinuations Due to Treatment-Limiting Toxicity (TLT)-Treatment Period (Part A)[10]

End point description:

AE=any new unfavorable symptom, sign, or disease or worsening of a preexisting condition that may not have a causal relationship with treatment. SAE=a medical event that at any dose results in death, persistent or significant disability/incapacity, or drug dependency/abuse; is life-threatening, an important medical event, or a congenital anomaly/birth defect; or requires or prolongs hospitalization. Treatment-related=having certain, probable, possible, or unknown relationship to study drug. Grade (Gr) 1=Mild, Gr 2=Moderate, Gr 3=Severe, Gr 4=Life-threatening or disabling. Analysis population included all treated subjects.

End point type	Secondary

End point timeframe:

Day 1 to end of treatment plus 10 days

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 only the specified arms.

End point values	Part A: Peginterferon Lambda 240 µg	Part A: Peginterferon Lambda 180 µg	Part A: Peginterferon alfa-2a 180 µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	80	83	
Units: Subjects				
SAEs	3	7	5	
Discontinuations Due to AEs	3	6	8	
AEs Leading to Dose Reduction	3	10	23	
Grade 1 to 4 AEs	13	76	77	
Grade 3 to 4 AEs	7	22	23	
Discontinuations due to TLT	2	5	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Grade 3 or 4 On-Treatment Emergent Laboratory Abnormalities - Part A

End point title	Number of Subjects With Grade 3 or 4 On-Treatment Emergent Laboratory Abnormalities - Part A[11]

End point description:

Laboratory tests with Division of AIDS (DAIDS) Version 1.0 toxicity criteria were performed and assessed. Platelet count: <50,000/mm^3; Leukocytes: <1500/mm^3; Lymphocytes (Absolute):<500/mm^3; Neutrophils+band (Absolute): <750/mm^3; Alanine transaminase (ALT): >5*upper limit of normal (ULN); Aspartate aminotransferase (AST): >5*ULN; Bilirubin (Total): >2.5*ULN; Bilirubin (direct): >3*ULN; Lipase, total: >3*ULN. Subjects with any grade 3 or 4 laboratory abnormalities are summarised. Analysis population included all treated subjects. Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms.

End point type	Secondary

End point timeframe:

Day 1 to end of treatment plus 10 days

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 only the specified arms.

End point values	Part A: Peginterferon Lambda 240 µg	Part A: Peginterferon Lambda 180 µg	Part A: Peginterferon alfa-2a 180 µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	80	83	
Units: Subjects				
Platelet count (n=13, 80, 82)	0	0	1	
Leukocytes (n=13, 80, 82)	0	0	1	
Lymphocytes (Absolute) (n=13, 80, 82)	0	1	1	
Neutrophils + band (Absolute) (n=13, 80, 82)	0	2	17	
ALT (n=13, 80, 82)	7	33	19	
AST (n=13, 80, 82)	7	27	15	
Bilirubin, total (n=13, 80, 82)	3	3	0	
Bilurubin, direct (n=7, 20, 5)	3	4	0	
Lipase, total (n=13, 80, 81)	0	0	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum observed concentration (Cmax) - Part A

End point title	Maximum observed concentration (Cmax) - Part A[12]

End point description:

Cmax is the peak plasma concentration of a drug after administration, obtained directly from the plasma concentration-time curve. Analysis population included all treated subjects. Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms.

End point type	Secondary

End point timeframe:

Day 1 and Day 85: pre-dose, 1, 2, 4, and 8 hours post-dose

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 only the specified arms.

End point values	Part A: Peginterferon Lambda 180 µg	Part A: Peginterferon alfa-2a 180 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Day 1 (n=4, 4)	1.48 (± 49.9)	5.08 (± 68.9)		
Day 85 (n=3, 3)	2.38 (± 65.1)	10.3 (± 26.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time of maximum observed concentration (Tmax) - Part A

End point title	Time of maximum observed concentration (Tmax) - Part A[13]

End point description:

Tmax: Time to reach the maximum plasma concentration. Analysis population included all treated subjects. Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms.

End point type	Secondary

End point timeframe:

Day 1 and Day 85: pre-dose, 1, 2, 4, and 8 hours post-dose

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 only the specified arms.

End point values	Part A: Peginterferon Lambda 180 µg	Part A: Peginterferon alfa-2a 180 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: hour				
median (full range (min-max))				
Day 1 (n=4, 4)	8 (4.52 to 24)	96 (48 to 144)		
Day 85 (n=3, 3)	24 (8 to 24)	72 (1.98 to 144)		

Statistical analyses

No statistical analyses for this end point

Secondary: Minimal Observed Plasma Concentration (Cmin) - Part A

End point title	Minimal Observed Plasma Concentration (Cmin) - Part A[14]

End point description:

Cmin: Minimal observed serum/plasma concentration. Analysis population included all treated subjects. Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms.

End point type	Secondary

End point timeframe:

Day 85: pre-dose, 1, 2, 4, and 8 hours post-dose

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 only the specified arms.

End point values	Part A: Peginterferon Lambda 180 µg	Part A: Peginterferon alfa-2a 180 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	3		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Day 85	0.243 (± 63)	6.43 (± 65.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration Time Curve in one Dosing Interval [AUC(TAU)] - Part A

End point title	Area Under the Concentration Time Curve in one Dosing Interval [AUC(TAU)] - Part A[15]

End point description:

AUC(TAU): Area under the serum/plasma concentration-time curve during one dose interval. Analysis population included all treated subjects. Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms.

End point type	Secondary

End point timeframe:

Day 1 and Day 85: pre-dose, 1, 2, 4, and 8 hours post-dose

Notes:

[15] - 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 only the specified arms.

End point values	Part A: Peginterferon Lambda 180 µg	Part A: Peginterferon alfa-2a 180 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: nanogram*hour per mililitre (ng*h/mL)				
geometric mean (geometric coefficient of variation)				
Day 1 (n=4, 4)	107 (± 38.5)	99999 (± 99999)		
Day 85 (n=4, 3)	188 (± 72.8)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Accumulation Index (AI): Ratio of AUC(TAU) at Steady-State to AUC(TAU) - Part A

End point title	Accumulation Index (AI): Ratio of AUC(TAU) at Steady-State to AUC(TAU) - Part A[16]

End point description:

AI: ratio of AUC(TAU) at steady-state to AUC(TAU) after the first dose. Analysis population included all treated subjects. Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms and '99999' represents not estimable data for specified categories in respective arms.

End point type	Secondary

End point timeframe:

Day 1 and Day 85: pre-dose, 1, 2, 4, and 8 hours post-dose

Notes:

[16] - 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 only the specified arms.

End point values	Part A: Peginterferon Lambda 180 µg	Part A: Peginterferon alfa-2a 180 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: Ratio				
geometric mean (geometric coefficient of variation)				
Day 85	1.52 (± 67.6)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieved HBeAg Seroconversion at Follow-up Week 24 – Part B

End point title	Percentage of Subjects Who Achieved HBeAg Seroconversion at Follow-up Week 24 – Part B[17]

End point description:

HBeAG seroconversion was defined as having a post-baseline negative serum HBeAg and simultaneous positive HBeAb for subjects with positive serum HBeAg and negative HBeAb at screening. The analysis was performed in all treated subjects.

End point type	Secondary

End point timeframe:

Follow-up Week 24

Notes:

[17] - 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 only the specified arms.

End point values	Part B: Peginterferon Lambda + Entecavir			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Percentage of subjects				
number (confidence interval 95%)	0 (0 to 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With HBV DNA <50 IU/mL - Part B

End point title	Percentage of Subjects With HBV DNA <50 IU/mL - Part B[18]

End point description:

HBV DNA was measured by PCR using the Roche COBAS TaqMan - HPS assay with LOQ = 29 IU/mL and LOD = 10 IU/mL. The analysis was performed in all treated subjects. Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms and '99999' represents not estimable data for specified categories in respective arms.

End point type	Secondary

End point timeframe:

Weeks 4, 8, 12, 36, 60, and 84

Notes:

[18] - 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 only the specified arms.

End point values	Part B: Peginterferon Lambda + Entecavir			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Percentage of subjects				
number (confidence interval 95%)				
Week 4 (n=13)	0 (0 to 0)			
Week 8 (n=13)	0 (0 to 0)			
Week 12 (n=12)	0 (0 to 0)			
Week 24 (n=8)	37.5 (8.5 to 75.5)			
Week 36 (n=5)	60 (14.7 to 94.7)			
Week 60 (n=0)	99999 (99999 to 99999)			
Week 84 (n=0)	99999 (99999 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Log10 HBV DNA levels - Part B

End point title	Mean Change From Baseline in Log10 HBV DNA levels - Part

End point description:

HBV DNA was measured by PCR using the Roche COBAS TaqMan - HPS assay with LOQ = 29 IU/mL and LOD = 10 IU/mL. Values below LOQ were set to LOQ-1. HBV DNA levels were converted to the log10 scale. Analysis population included all treated subjects.

End point type	Secondary

End point timeframe:

Baseline and at Weeks 4, 8, 12, 24, 36, 60, 84

Notes:

[19] - 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 only the specified arms.

End point values	Part B: Peginterferon Lambda + Entecavir			
Subject group type	Reporting group			
Number of subjects analysed	0[20]			
Units: Log 10 IU/mL				
arithmetic mean (standard deviation)	()			

Notes:

[20] - This endpoint was planned but not analyzed due to early study termination

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with ALT Normalization – Part B

End point title	Percentage of Subjects with ALT Normalization – Part B[21]

End point description:

ALT normalization was defined as having ALT values <=1*ULN for subjects who have values >ULN at screening. Values below LOQ were set to LOQ-1. The analysis was performed in all treated subjects. Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms and '99999' represents not estimable data for specified categories in respective arms.

End point type	Secondary

End point timeframe:

Weeks 4, 8, 12, 24, 36, 60, 84

Notes:

[21] - 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 only the specified arms.

End point values	Part B: Peginterferon Lambda + Entecavir			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Percentage of subjects				
number (confidence interval 95%)				
Week 4 (n=13)	7.7 (0.2 to 36)			
Week 8 (n=13)	23.1 (5 to 53.8)			
Week 12 (n=13)	38.5 (13.9 to 68.4)			
Week 24 (n=9)	33.3 (7.5 to 70.1)			
Week 36 (n=5)	60 (14.7 to 94.7)			
Week 60 (n=0)	99999 (99999 to 99999)			
Week 84 (n=0)	99999 (99999 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With HBeAg Loss - Part B

End point title	Percentage of Subjects With HBeAg Loss - Part B[22]

End point description:

HBeAg loss was defined as having negative post-baseline serum HBeAg for subjects with positive serum HBeAg at screening. Values below LOQ were set to LOQ-1. HBeAG levels were measured using commercially available quantitative HBeAg (qHBeAg) assays (ARCHITECT [Abbott]). The analysis was performed in all treated subjects. Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms and '99999' represents not estimable data for specified categories in respective arms.

End point type	Secondary

End point timeframe:

Weeks 12, 24, 36, 60, and 84

Notes:

[22] - 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 only the specified arms.

End point values	Part B: Peginterferon Lambda + Entecavir			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Percentage of subjects				
number (confidence interval 95%)				
Week 12 (n=13)	0 (0 to 0)			
Week 24 (n=8)	0 (0 to 0)			
Week 36 (n=5)	0 (0 to 0)			
Week 60 (n=0)	99999 (99999 to 99999)			
Week 84 (n=0)	99999 (99999 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With HBeAg Seroconversion - Part B

End point title	Percentage of Subjects With HBeAg Seroconversion - Part B[23]

End point description:

HBeAG seroconversion was defined as having a post-baseline negative serum HBeAg and simultaneous positive HBeAb for subjects with positive serum HBeAg and negative HBeAb at screening. The analysis was performed in all treated subjects. Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms and '99999' represents not estimable data for specified categories in respective arms.

End point type	Secondary

End point timeframe:

Weeks 12, 24, 36, 60, and 84

Notes:

[23] - 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 only the specified arms.

End point values	Part B: Peginterferon Lambda + Entecavir			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Percentage of subjects				
number (confidence interval 95%)				
Week 12 (n=13)	0 (0 to 0)			
Week 24 (n=8)	0 (0 to 0)			
Week 36 (n=5)	0 (0 to 0)			
Week 60 (n=0)	99999 (99999 to 99999)			
Week 84 (n=0)	99999 (99999 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Log10 Quantitative HBeAg - Part B

End point title	Mean Change From Baseline in Log10 Quantitative HBeAg - Part B[24]

End point description:

HBeAG levels were measured using commercially available quantitative HBeAg (qHBeAg) assays (ARCHITECT [Abbott]). The dynamic range of the qHBeAg assay is 0.22-56.70 PEI U/mL and the assay is currently validated to dilute samples with a concentration of up to 567 PEI U/mL. Values below the lower LOQ were set to lower LOQ/2. Values above the upper LOQ were set to upper LOQ+1. qHBeAg values were converted to the log 10 scale. Analysis population included all treated subjects. Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms and '99999' represents not estimable data for specified categories in respective arms.

End point type	Secondary

End point timeframe:

Weeks 12, 24, 36, 60, and 84

Notes:

[24] - 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 only the specified arms.

End point values	Part B: Peginterferon Lambda + Entecavir			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Log 10 IU/mL				
arithmetic mean (standard deviation)				
Week 12 (n=13)	-0.0465 (± 0.47483)			
Week 24 (n=8)	-0.8293 (± 0.87189)			
Week 36 (n=4)	-0.87 (± 1.16781)			
Week 60 (n=0)	99999 (± 99999)			
Week 84 (n=0)	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Grade 3 or 4 On-Treatment Emergent

Laboratory Abnormalities - Part B

End point title	Number of Subjects With Grade 3 or 4 On-Treatment Emergent Laboratory Abnormalities - Part B[25]

End point description:

Laboratory tests with DAIDS Version 1.0 toxicity criteria were performed and assessed. ALT: >5*ULN; AST: >5*ULN. Analysis population included all treated subjects.

End point type	Secondary

End point timeframe:

Day 1 to end of treatment plus 10 days

Notes:

[25] - 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 only the specified arms.

End point values	Part B: Peginterferon Lambda + Entecavir			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Subjects				
ALT	3			
AST	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With SAEs, Discontinuations Due to AEs, Grade 1 to 4 AEs, Grade 3 to 4 AEs and who Died - Part B

End point title	Number of Subjects With SAEs, Discontinuations Due to AEs, Grade 1 to 4 AEs, Grade 3 to 4 AEs and who Died - Part B[26]

End point description:

AE=any new unfavorable symptom, sign, or disease or worsening of a preexisting condition that may not have a causal relationship with treatment. SAE=a medical event that at any dose results in death, persistent or significant disability/incapacity, or drug dependency/abuse; is life-threatening, an important medical event, or a congenital anomaly/birth defect; or requires or prolongs hospitalization. Treatment-related=having certain, probable, possible, or unknown relationship to study drug. Grade (Gr) 1=Mild, Gr 2=Moderate, Gr 3=Severe, Gr 4=Life-threatening or disabling. Analysis population included all treated subjects.

End point type	Secondary

End point timeframe:

Day 1 to end of treatment plus 10 days

Notes:

[26] - 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 only the specified arms.

End point values	Part B: Peginterferon Lambda + Entecavir			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Subjects				
SAEs	0			
Discontinuations due to AEs	0			
Grade 1 to 4 AEs	8			
Grade 3 to 4 AEs	1			
Deaths	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with SAEs - Follow-up Period (Part A)

End point title	Number of Subjects with SAEs - Follow-up Period (Part A)

End point description:

SAE=a medical event that at any dose results in death, persistent or significant disability/incapacity, or drug dependency/abuse; is life-threatening, an important medical event, or a congenital anomaly/birth defect; or requires or prolongs hospitalization.

End point type	Secondary

End point timeframe:

From start of study treatment to 24-week post-dosing follow-up visit (up to Week 72)

End point values	Part A: Peginterferon Lambda 240 µg	Part A: Peginterferon Lambda 180 µg	Part A: Peginterferon alfa-2a 180 µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	78	78	
Units: subjects	1	7	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects experiencing anti-drug antibody (ADA) seroconversion or boosted ADA response on treatment

End point title	Number of subjects experiencing anti-drug antibody (ADA) seroconversion or boosted ADA response on treatment[27]

End point description:

Subjects were assessed for the presence of anti-drug (interferon) antibodies at baseline and during the course of study therapy. Subjects who had detectable antibodies at
baseline were assessed for change (increase or boosting) of antibody titer during treatment.

End point type	Secondary

End point timeframe:

Day 1 to Week 24 Follow-up visit

Notes:

[27] - 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 only the specified arms.

End point values	Part A: Peginterferon Lambda 240 µg	Part A: Peginterferon Lambda 180 µg	Part A: Peginterferon alfa-2a 180 µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13[28]	80[29]	83[30]	
Units: subjects				
Subjects who seroconverted	6	45	27	
Subjects with a boosted response	1	2	0	

Notes:

[28] - Subjects with anti-drug antibodies tested at baseline

[29] - Subjects with anti-drug antibodies tested at baseline

[30] - Subjects with anti-drug antibodies tested at baseline

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Day 1 through the end of treatment plus 10 days	
Adverse event reporting additional description:	
On-treatment period.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups	
Reporting group title	Part A: Peginterferon Lambda 240 µg
Reporting group description:	
Subjects received Peginterferon Lambda 240 µg, subcutaneous, once weekly for 48 weeks.	
Reporting group title	Part A: Peginterferon Lambda 180 µg
Reporting group description:	
Subjects received Peginterferon Lambda 180 µg, subcutaneous, once weekly for 48 weeks.	
Reporting group title	Part A: Peginterferon alfa-2a 180 µg
Reporting group description:	
Subjects received Peginterferon alfa-2a 180 µg, subcutaneous, once weekly for 48 weeks.	
Reporting group title	Part B: Peginterferon Lambda + Entecavir
Reporting group description:	
Subjects with hepatitis E antigen-positive (HBeAg-positive) chronic hepatitis B virus (HBV) infection received Entecavir 0.5 mg, tablets, orally, once daily for 12 weeks; Peginterferon Lambda 180 µg, subcutaneous, once weekly along with Entecavir 0.5 mg, tablets, orally, once daily for 48 weeks.	
Reporting group title	Part B: Entecavir
Reporting group description:	
Subjects with hepatitis E antigen-positive (HBeAg-positive) chronic hepatitis B virus (HBV) infection received Entecavir 0.5 mg, tablets, orally, once daily for up to 12 weeks.	

Serious adverse events	Part A: Peginterferon Lambda 240 µg	Part A: Peginterferon Lambda 180 µg	Part A: Peginterferon alfa-2a 180 µg
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 13 (23.08%)	7 / 80 (8.75%)	5 / 83 (6.02%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 13 (7.69%)	2 / 80 (2.50%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	1 / 1	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			

subjects affected / exposed	0 / 13 (0.00%)	1 / 80 (1.25%)	0 / 83 (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
Cardiac disorders			
Coronary artery stenosis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 80 (0.00%)	0 / 83 (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
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 80 (0.00%)	1 / 83 (1.20%)
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 disorders			
Gastric ulcer			
subjects affected / exposed	0 / 13 (0.00%)	1 / 80 (1.25%)	0 / 83 (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
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	1 / 13 (7.69%)	1 / 80 (1.25%)	1 / 83 (1.20%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperbilirubinaemia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 80 (0.00%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal hypertension			
subjects affected / exposed	1 / 13 (7.69%)	0 / 80 (0.00%)	0 / 83 (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
Musculoskeletal and connective tissue disorders			
Back pain			

subjects affected / exposed	0 / 13 (0.00%)	1 / 80 (1.25%)	1 / 83 (1.20%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 13 (0.00%)	0 / 80 (0.00%)	1 / 83 (1.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 80 (1.25%)	0 / 83 (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
Pyelonephritis acute			
subjects affected / exposed	0 / 13 (0.00%)	1 / 80 (1.25%)	0 / 83 (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
Pulmonary tuberculosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 80 (0.00%)	1 / 83 (1.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 80 (0.00%)	1 / 83 (1.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part B: Peginterferon Lambda + Entecavir	Part B: Entecavir	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood bilirubin increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Coronary artery stenosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastric ulcer			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperbilirubinaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal hypertension			

subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	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	Part A: Peginterferon Lambda 240 µg	Part A: Peginterferon Lambda 180 µg	Part A: Peginterferon alfa-2a 180 µg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 13 (100.00%)	72 / 80 (90.00%)	74 / 83 (89.16%)
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 13 (7.69%)	2 / 80 (2.50%)	2 / 83 (2.41%)
occurrences (all)	1	3	2
Chills			
subjects affected / exposed	0 / 13 (0.00%)	2 / 80 (2.50%)	8 / 83 (9.64%)
occurrences (all)	0	2	9
Fatigue			
subjects affected / exposed	4 / 13 (30.77%)	26 / 80 (32.50%)	24 / 83 (28.92%)
occurrences (all)	4	30	26
Influenza like illness			
subjects affected / exposed	1 / 13 (7.69%)	4 / 80 (5.00%)	8 / 83 (9.64%)
occurrences (all)	1	7	11
Injection site erythema			
subjects affected / exposed	0 / 13 (0.00%)	1 / 80 (1.25%)	7 / 83 (8.43%)
occurrences (all)	0	1	7
Injection site pruritus			
subjects affected / exposed	1 / 13 (7.69%)	3 / 80 (3.75%)	0 / 83 (0.00%)
occurrences (all)	2	3	0
Injection site rash			
subjects affected / exposed	2 / 13 (15.38%)	7 / 80 (8.75%)	2 / 83 (2.41%)
occurrences (all)	2	7	2
Injection site reaction			
subjects affected / exposed	0 / 13 (0.00%)	1 / 80 (1.25%)	5 / 83 (6.02%)
occurrences (all)	0	1	5
Injection site swelling			
subjects affected / exposed	0 / 13 (0.00%)	0 / 80 (0.00%)	0 / 83 (0.00%)
occurrences (all)	0	0	0
Irritability			
subjects affected / exposed	2 / 13 (15.38%)	0 / 80 (0.00%)	3 / 83 (3.61%)
occurrences (all)	2	0	3
Malaise			

subjects affected / exposed	0 / 13 (0.00%)	10 / 80 (12.50%)	3 / 83 (3.61%)
occurrences (all)	0	17	9
Pyrexia			
subjects affected / exposed	2 / 13 (15.38%)	8 / 80 (10.00%)	37 / 83 (44.58%)
occurrences (all)	4	21	49
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	0 / 80 (0.00%)	0 / 83 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 13 (0.00%)	6 / 80 (7.50%)	8 / 83 (9.64%)
occurrences (all)	0	9	13
Dyspnoea			
subjects affected / exposed	1 / 13 (7.69%)	1 / 80 (1.25%)	5 / 83 (6.02%)
occurrences (all)	1	1	5
Oropharyngeal pain			
subjects affected / exposed	2 / 13 (15.38%)	5 / 80 (6.25%)	5 / 83 (6.02%)
occurrences (all)	2	5	6
Rhinitis allergic			
subjects affected / exposed	2 / 13 (15.38%)	0 / 80 (0.00%)	1 / 83 (1.20%)
occurrences (all)	2	0	1
Throat tightness			
subjects affected / exposed	1 / 13 (7.69%)	0 / 80 (0.00%)	0 / 83 (0.00%)
occurrences (all)	1	0	0
Wheezing			
subjects affected / exposed	1 / 13 (7.69%)	0 / 80 (0.00%)	0 / 83 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 13 (7.69%)	3 / 80 (3.75%)	3 / 83 (3.61%)
occurrences (all)	1	3	4
Insomnia			
subjects affected / exposed	1 / 13 (7.69%)	8 / 80 (10.00%)	10 / 83 (12.05%)
occurrences (all)	1	9	10
Sleep disorder			

subjects affected / exposed	0 / 13 (0.00%)	2 / 80 (2.50%)	2 / 83 (2.41%)
occurrences (all)	0	2	2
Somnambulism			
subjects affected / exposed	1 / 13 (7.69%)	0 / 80 (0.00%)	0 / 83 (0.00%)
occurrences (all)	1	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	4 / 13 (30.77%)	14 / 80 (17.50%)	8 / 83 (9.64%)
occurrences (all)	6	21	8
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 13 (15.38%)	7 / 80 (8.75%)	6 / 83 (7.23%)
occurrences (all)	3	8	6
Blood bilirubin increased			
subjects affected / exposed	1 / 13 (7.69%)	1 / 80 (1.25%)	0 / 83 (0.00%)
occurrences (all)	1	1	0
Blood glucose increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 80 (0.00%)	0 / 83 (0.00%)
occurrences (all)	1	0	0
Hepatic enzyme increased			
subjects affected / exposed	1 / 13 (7.69%)	1 / 80 (1.25%)	0 / 83 (0.00%)
occurrences (all)	1	1	0
Neutrophil count decreased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 80 (1.25%)	9 / 83 (10.84%)
occurrences (all)	0	1	11
Transaminases increased			
subjects affected / exposed	1 / 13 (7.69%)	3 / 80 (3.75%)	2 / 83 (2.41%)
occurrences (all)	2	4	3
Injury, poisoning and procedural complications			
Limb crushing injury			
subjects affected / exposed	1 / 13 (7.69%)	0 / 80 (0.00%)	0 / 83 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Gastrocardiac syndrome			
subjects affected / exposed	1 / 13 (7.69%)	0 / 80 (0.00%)	0 / 83 (0.00%)
occurrences (all)	1	0	0
Palpitations			

subjects affected / exposed	1 / 13 (7.69%)	1 / 80 (1.25%)	2 / 83 (2.41%)
occurrences (all)	1	1	2
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	0 / 13 (0.00%)	0 / 80 (0.00%)	2 / 83 (2.41%)
occurrences (all)	0	0	3
Dizziness			
subjects affected / exposed	0 / 13 (0.00%)	5 / 80 (6.25%)	13 / 83 (15.66%)
occurrences (all)	0	6	23
Headache			
subjects affected / exposed	4 / 13 (30.77%)	11 / 80 (13.75%)	24 / 83 (28.92%)
occurrences (all)	5	21	50
Lethargy			
subjects affected / exposed	1 / 13 (7.69%)	2 / 80 (2.50%)	2 / 83 (2.41%)
occurrences (all)	2	2	3
Myoclonus			
subjects affected / exposed	1 / 13 (7.69%)	0 / 80 (0.00%)	0 / 83 (0.00%)
occurrences (all)	1	0	0
Somnolence			
subjects affected / exposed	1 / 13 (7.69%)	0 / 80 (0.00%)	0 / 83 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 80 (0.00%)	7 / 83 (8.43%)
occurrences (all)	0	0	8
Lymphadenopathy			
subjects affected / exposed	1 / 13 (7.69%)	0 / 80 (0.00%)	0 / 83 (0.00%)
occurrences (all)	1	0	0
Neutropenia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 80 (0.00%)	20 / 83 (24.10%)
occurrences (all)	0	0	25
Thrombocytopenia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 80 (1.25%)	5 / 83 (6.02%)
occurrences (all)	0	1	6
Eye disorders			

Blindness transient			
subjects affected / exposed	1 / 13 (7.69%)	0 / 80 (0.00%)	0 / 83 (0.00%)
occurrences (all)	1	0	0
Eye pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 80 (0.00%)	1 / 83 (1.20%)
occurrences (all)	1	0	1
Visual acuity reduced			
subjects affected / exposed	1 / 13 (7.69%)	0 / 80 (0.00%)	1 / 83 (1.20%)
occurrences (all)	1	0	1
Gastrointestinal disorders			
Dry mouth			
subjects affected / exposed	0 / 13 (0.00%)	1 / 80 (1.25%)	0 / 83 (0.00%)
occurrences (all)	0	1	0
Abdominal discomfort			
subjects affected / exposed	1 / 13 (7.69%)	0 / 80 (0.00%)	1 / 83 (1.20%)
occurrences (all)	1	0	1
Abdominal distension			
subjects affected / exposed	2 / 13 (15.38%)	4 / 80 (5.00%)	1 / 83 (1.20%)
occurrences (all)	3	4	1
Abdominal pain			
subjects affected / exposed	1 / 13 (7.69%)	4 / 80 (5.00%)	4 / 83 (4.82%)
occurrences (all)	1	4	4
Abdominal pain upper			
subjects affected / exposed	1 / 13 (7.69%)	8 / 80 (10.00%)	7 / 83 (8.43%)
occurrences (all)	1	12	10
Constipation			
subjects affected / exposed	0 / 13 (0.00%)	4 / 80 (5.00%)	4 / 83 (4.82%)
occurrences (all)	0	4	4
Diarrhoea			
subjects affected / exposed	2 / 13 (15.38%)	5 / 80 (6.25%)	8 / 83 (9.64%)
occurrences (all)	2	5	20
Flatulence			
subjects affected / exposed	1 / 13 (7.69%)	0 / 80 (0.00%)	0 / 83 (0.00%)
occurrences (all)	1	0	0
Gingival polyp			

subjects affected / exposed	1 / 13 (7.69%)	0 / 80 (0.00%)	0 / 83 (0.00%)
occurrences (all)	1	0	0
Haematochezia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 80 (0.00%)	0 / 83 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	0 / 13 (0.00%)	0 / 80 (0.00%)	8 / 83 (9.64%)
occurrences (all)	0	0	9
Nausea			
subjects affected / exposed	3 / 13 (23.08%)	12 / 80 (15.00%)	7 / 83 (8.43%)
occurrences (all)	8	14	11
Vomiting			
subjects affected / exposed	0 / 13 (0.00%)	7 / 80 (8.75%)	4 / 83 (4.82%)
occurrences (all)	0	9	5
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	1 / 13 (7.69%)	1 / 80 (1.25%)	0 / 83 (0.00%)
occurrences (all)	1	1	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 13 (0.00%)	9 / 80 (11.25%)	25 / 83 (30.12%)
occurrences (all)	0	9	27
Dry skin			
subjects affected / exposed	1 / 13 (7.69%)	3 / 80 (3.75%)	2 / 83 (2.41%)
occurrences (all)	1	3	2
Eczema			
subjects affected / exposed	0 / 13 (0.00%)	0 / 80 (0.00%)	4 / 83 (4.82%)
occurrences (all)	0	0	4
Night sweats			
subjects affected / exposed	1 / 13 (7.69%)	0 / 80 (0.00%)	1 / 83 (1.20%)
occurrences (all)	1	0	2
Pruritus			
subjects affected / exposed	0 / 13 (0.00%)	7 / 80 (8.75%)	13 / 83 (15.66%)
occurrences (all)	0	12	14
Rash			

subjects affected / exposed	0 / 13 (0.00%)	4 / 80 (5.00%)	12 / 83 (14.46%)
occurrences (all)	0	4	13
Skin reaction			
subjects affected / exposed	1 / 13 (7.69%)	0 / 80 (0.00%)	0 / 83 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 13 (15.38%)	0 / 80 (0.00%)	10 / 83 (12.05%)
occurrences (all)	2	0	12
Back pain			
subjects affected / exposed	0 / 13 (0.00%)	5 / 80 (6.25%)	4 / 83 (4.82%)
occurrences (all)	0	6	7
Musculoskeletal pain			
subjects affected / exposed	1 / 13 (7.69%)	2 / 80 (2.50%)	1 / 83 (1.20%)
occurrences (all)	2	2	1
Myalgia			
subjects affected / exposed	2 / 13 (15.38%)	3 / 80 (3.75%)	18 / 83 (21.69%)
occurrences (all)	2	3	23
Tenosynovitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 80 (0.00%)	0 / 83 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 80 (0.00%)	1 / 83 (1.20%)
occurrences (all)	1	0	1
Influenza			
subjects affected / exposed	0 / 13 (0.00%)	5 / 80 (6.25%)	5 / 83 (6.02%)
occurrences (all)	0	14	6
Nasopharyngitis			
subjects affected / exposed	0 / 13 (0.00%)	4 / 80 (5.00%)	2 / 83 (2.41%)
occurrences (all)	0	7	4
Periodontitis			
subjects affected / exposed	1 / 13 (7.69%)	1 / 80 (1.25%)	0 / 83 (0.00%)
occurrences (all)	1	1	0
Upper respiratory tract infection			

subjects affected / exposed	1 / 13 (7.69%)	4 / 80 (5.00%)	6 / 83 (7.23%)
occurrences (all)	2	8	12
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 13 (23.08%)	3 / 80 (3.75%)	9 / 83 (10.84%)
occurrences (all)	3	4	10
Hypophagia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 80 (0.00%)	0 / 83 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Part B: Peginterferon Lambda + Entecavir	Part B: Entecavir	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 13 (61.54%)	2 / 8 (25.00%)	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Chills			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Fatigue			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Influenza like illness			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Injection site erythema			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Injection site pruritus			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Injection site rash			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Injection site reaction			

subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Injection site swelling			
subjects affected / exposed	1 / 13 (7.69%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Irritability			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Malaise			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Pyrexia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Dyspnoea			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Rhinitis allergic			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Throat tightness			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Wheezing			

subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Insomnia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Sleep disorder			
subjects affected / exposed	1 / 13 (7.69%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Somnambulism			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Blood bilirubin increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Blood glucose increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Hepatic enzyme increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Neutrophil count decreased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Transaminases increased			

subjects affected / exposed	1 / 13 (7.69%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Limb crushing injury			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Gastrocardiac syndrome			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Palpitations			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	1 / 13 (7.69%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	1 / 13 (7.69%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	1 / 13 (7.69%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Lethargy			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Myoclonus			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Somnolence			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	

Lymphadenopathy			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Neutropenia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Thrombocytopenia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Blindness transient			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Eye pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Visual acuity reduced			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Dry mouth			
subjects affected / exposed	0 / 13 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Abdominal discomfort			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Abdominal distension			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Abdominal pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Abdominal pain upper			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Constipation			

subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Diarrhoea			
subjects affected / exposed	1 / 13 (7.69%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Flatulence			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Gingival polyp			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Haematochezia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Mouth ulceration			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	1 / 13 (7.69%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Dry skin			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Eczema			

subjects affected / exposed	2 / 13 (15.38%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Night sweats			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Pruritus			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Rash			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Skin reaction			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Back pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Myalgia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Tenosynovitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Influenza			

subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Nasopharyngitis			
subjects affected / exposed	2 / 13 (15.38%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Periodontitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Hypophagia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 February 2011	The purpose of this amendment was to: • Add clarification on all subjects who discontinue from study therapy early to receive 24 week follow-up, • Update Overall Risk/Benefit Assessment which outlines significant level hyperbilirubinemia as a potential safety signal for pegIFN λ,
18 April 2011	• Dropped the 240 µg arm and modified hypothesis and study design to eliminate dose ranging, and changed the number of subjects from 180 to 170, • Changed study rationale to reflect outcome from the Week 12 interim analysis of the 2b phase of the ongoing study AI452-004 (EMERGE), • Added sections to describe the AI452-004 (EMERGE) study, and the safety and efficacy of the 240 µg vs 180 µg doses, • Made changes in regards to safety and management of lab abnormalities, • Changed design to reflect a 1:1 arm randomisation instead of 1:1:1, and dropped the 240 µg arm,
23 May 2011	• Added language pertaining to the ALT inclusion criteria for study, • Addition of Netherlands as a participating country, • Inserted additional risks associated with IFN α, • Inserted language pertaining to ALT flares for patients with chronic HBV infection, • Updated ALT criteria to >47 U/L to <10*ULN, • Added contraception be used for 24 weeks during post dosing for women of childbearing potential (WOCBP), • Changed weekly pregnancy testing to "at least monthly" to be consistent with requirements for pegIFN monotherapy, • Modified to exclude subjects only with severe psychiatric disease and allow subjects with either mild or moderate depression , • Replaced serum albumin <LLN with <=3.5 g/dl, • Removed fibrinogen as an eligibility criterion; maintained as an on study laboratory assessment, • Changed prior investigational product usage from 60 to 30 days prior to randomisation, • Changed prior hematologic growth factors use from 60 to 30 days prior to randomisation, • Language modified in selection and timing of dose of each subject and to specify the criteria for treatment interruption, dose reduction and discontinuation due to hepatobiliary events; in addition guidelines were provided on laboratory monitoring, • Added a Week 8 HBV DNA assessment, • Updated the dual lab testing at local and central lab to occur only at Weeks 1, 2, 3, 4, and 8, • Provided criteria for the definition and reporting of potential drug-induced liver injury (DILI).
06 September 2011	• Added FibroTest assessment at screening as an option to determine baseline liver status when historical liver biopsy data is not available, • Edited ALT/AST criteria requiring immediate discontinuation, • Included immediate discontinuation criteria (if Creatinine Clearance is < 50 mL/min), • Added FibroTest as means of evaluating for presence/absence of cirrhosis, • Edited screening period for this study from 28 days to 28 days (± 3 days) and subsequent dosing of randomised subjects within 28 days (± 3 days) of the day they are screened.

05 April 2012	• Added a potential of five additional long term follow-up visits to the post dosing follow-up, • Added criteria for which subjects would be eligible for long term follow-up, • Edited the Study Schema, • Added criteria when the medical monitor should be contacted for dose modifications due to adverse events and laboratory abnormalities, • Clarified in the short term procedures that serum samples should be provided for interferon antibody and pharmacokinetic trough samples, • Added weeks 96, 120, 144, 168, and 192 to the long term procedures table, • Updated adverse event reporting to include up to Week 192 post dosing.
08 January 2013	• Clarified post dosing follow-up requirements for subjects and site staff.
24 May 2013	• Removed incorrect Branding name for study (removed incorrect study name and inserted correct, LIRA-B), • Clarified Clinical Outcomes reporting.

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 treatment failed to meet the pre-specified non-inferiority criteria for the primary endpoint and several key secondary efficacy endpoints. Hence, the sponsor decided to terminate the ongoing long-term follow-up phase and Part B sub-study.

Notes: