Clinical trial results:
A Phase IIIb Parallel Group, Open Label Study of Pegylated Interferon Alfa-2a Monotherapy (PEG-IFN, Ro 25-8310) Compared to Untreated Control in Children with HBeAg Positive Chronic Hepatitis B in the Immune Active Phase

Summary

EudraCT number	2011-002732-70
Trial protocol	GB BE DE PL IT BG
Global end of trial date	18 October 2021

Results information

Result version number	v2 (current)
This version publication date	22 April 2022
First version publication date	24 July 2016
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	YV25718

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01519960
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, +41 61 6878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, +41 61 6878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000298-PIP01-08
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 November 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 October 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This randomized, controlled, parallel-group, open-label, multicenter study was designed to evaluate the use of peginterferon alfa-2a (PEG-IFN) monotherapy versus untreated control in pediatric participants with hepatitis B envelope antigen (HBeAg)-positive chronic hepatitis B (CHB) in the immune active phase. The study compared efficacy and safety between groups and evaluated the pharmacokinetics of PEG-IFN following administration of a body surface area (BSA)-based dosing regimen.

Protection of trial subjects:

The investigators have ensured that this study was conducted in full conformance with the principles of the Declaration of Helsinki or with the laws and regulations of the country in which the research was conducted, whichever afforded the greater protection to the individual. The study has fully adhered to the principles outlined in "Guideline for Good Clinical Practice" International Council for Harmonisation (ICH) Tripartite Guideline or with local law if it afforded greater protection to the participant. For studies conducted in the European Union (EU)/European Economic Area (EEA) countries, the investigators have ensured compliance with the EU Clinical Trial Directive (2001/20/EC). The investigators have additionally ensured adherence to the basic principles of "Good Clinical Practice" as outlined in the current version of 21 Code of Federal Regulations, subchapter D, part 312, "Responsibilities of Sponsors and Investigators"; part 50, "Protection of Human Subjects"; and part 56, "Institutional Review Boards". In other countries where "Guideline for Good Clinical Practice" exists, Roche and the investigators have strictly ensured adherence to the stated provisions.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 July 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Ethical reason, Regulatory reason, Scientific research
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Ukraine: 13
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	United States: 8
Country: Number of subjects enrolled	Australia: 10
Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	Bulgaria: 4
Country: Number of subjects enrolled	China: 76
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Israel: 9

Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Poland: 4
Country: Number of subjects enrolled	Russian Federation: 19
Worldwide total number of subjects	161
EEA total number of subjects	20

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)	82
Adolescents (12-17 years)	79
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 211 individuals were screened for entry into the study. Of these, there were 161 participants enrolled in the study and included in the main analyses.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis

Arm description:

Participants without advanced fibrosis were randomized and received PEG-IFN monotherapy for 48 weeks with a 24-week follow-up and an additional 4.5-year extended follow-up. Each dose of 45 to 180 micrograms (mcg) was based on BSA and given as a once-weekly subcutaneous (SC) injection for 48 weeks. BSA-based dosing was as follows: 0.51-0.53 square meters (m^2), 45 mcg; 0.54-0.74 m^2, 65 mcg; 0.75-1.08 m^2, 90 mcg; 1.09-1.51 m^2, 135 mcg; greater than (>) 1.51 m^2, 180 mcg.

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

Dosage and administration details:

Peginterferon alfa-2a was given as SC injection once weekly for 48 weeks and dosed according to BSA category as specified in the protocol. Possible doses ranged from 45 to 180 mcg.

Arm title	Group B: Untreated Control Without Advanced Fibrosis

Arm description:

Participants without advanced fibrosis were randomized and were evaluated for 48 weeks with a 24-week follow-up and an additional ongoing 4.5-year extended follow-up. As the study is open-label, participants did not receive any investigational or placebo treatment during the 48-week principal observation period (POP). For ethical reasons, participants in Group B had a reduced visit schedule (every 12 weeks) compared to participants in Group A through the end of 24-week follow-up. After completing the POP, the same PEG-IFN regimen administered in Group A was offered to participants in Group B who had not experienced hepatitis B envelope antigen (HBeAg) seroconversion. The offer remained for up to 1 year following the Week 48 visit. From the time a given participant switched to PEG-IFN, he/she was no longer included in Group B.

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

Dosage and administration details:

Peginterferon alfa-2a was given as SC injection once weekly for 48 weeks and dosed according to BSA category as specified in the protocol. Possible doses ranged from 45 to 180 mcg.

Arm title	Group C: PEG-IFN Monotherapy With Advanced Fibrosis

Arm description:

Participants with advanced fibrosis were allocated (not randomized) to receive PEG-IFN monotherapy for 48 weeks with a 24-week follow-up and an additional 4.5-year extended follow-up. Each dose of 45 to 180 mcg was based on BSA and given as a once-weekly SC injection for 48 weeks. BSA-based dosing was as follows: 0.51-0.53 m^2, 45 mcg; 0.54-0.74 m^2, 65 mcg; 0.75-1.08 m^2, 90 mcg; 1.09-1.51 m^2, 135 mcg; >1.51 m^2, 180 mcg.

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

Dosage and administration details:

Peginterferon alfa-2a was given as SC injection once weekly for 48 weeks and dosed according to BSA category as specified in the protocol. Possible doses ranged from 45 to 180 mcg.

Number of subjects in period 1	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis	Group C: PEG-IFN Monotherapy With Advanced Fibrosis
Started	101	50	10
Completed Week 48	99	47	10
Completed Follow-Up (FU) Week 12	99	26 [1]	10
Completed FU Week 24	99	15 [2]	10
Completed FU 5 year	75	28	5
Switch Group	0 [3]	33	0 [4]
Completed	75	28	5
Not completed	26	22	5
Withdrawal from the study	26	22	5

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.
[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.
[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.
[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

Baseline characteristics

Reporting groups	
Reporting group title	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis
Reporting group description:	
Participants without advanced fibrosis were randomized and received PEG-IFN monotherapy for 48 weeks with a 24-week follow-up and an additional 4.5-year extended follow-up. Each dose of 45 to 180 micrograms (mcg) was based on BSA and given as a once-weekly subcutaneous (SC) injection for 48 weeks. BSA-based dosing was as follows: 0.51-0.53 square meters (m^2), 45 mcg; 0.54-0.74 m^2, 65 mcg; 0.75-1.08 m^2, 90 mcg; 1.09-1.51 m^2, 135 mcg; greater than (>) 1.51 m^2, 180 mcg.	
Reporting group title	Group B: Untreated Control Without Advanced Fibrosis
Reporting group description:	
Participants without advanced fibrosis were randomized and were evaluated for 48 weeks with a 24-week follow-up and an additional ongoing 4.5-year extended follow-up. As the study is open-label, participants did not receive any investigational or placebo treatment during the 48-week principal observation period (POP). For ethical reasons, participants in Group B had a reduced visit schedule (every 12 weeks) compared to participants in Group A through the end of 24-week follow-up. After completing the POP, the same PEG-IFN regimen administered in Group A was offered to participants in Group B who had not experienced hepatitis B envelope antigen (HBeAg) seroconversion. The offer remained for up to 1 year following the Week 48 visit. From the time a given participant switched to PEG-IFN, he/she was no longer included in Group B.	
Reporting group title	Group C: PEG-IFN Monotherapy With Advanced Fibrosis
Reporting group description:	
Participants with advanced fibrosis were allocated (not randomized) to receive PEG-IFN monotherapy for 48 weeks with a 24-week follow-up and an additional 4.5-year extended follow-up. Each dose of 45 to 180 mcg was based on BSA and given as a once-weekly SC injection for 48 weeks. BSA-based dosing was as follows: 0.51-0.53 m^2, 45 mcg; 0.54-0.74 m^2, 65 mcg; 0.75-1.08 m^2, 90 mcg; 1.09-1.51 m^2, 135 mcg; >1.51 m^2, 180 mcg.	

Reporting group values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis	Group C: PEG-IFN Monotherapy With Advanced Fibrosis
Number of subjects	101	50	10
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	53	20	9
Adolescents (12-17 years)	48	30	1
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	10.41	11.2	6.7
standard deviation	± 4.57	± 5.01	± 3.27
Gender Categorical Units: Subjects			
Female	37	18	2
Male	64	32	8

Reporting group values	Total		
Number of subjects	161		
Age Categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	82		
Adolescents (12-17 years)	79		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender Categorical Units: Subjects			
Female	57		
Male	104		

End points

End points reporting groups

Reporting group title	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis

Reporting group description:

Participants without advanced fibrosis were randomized and received PEG-IFN monotherapy for 48 weeks with a 24-week follow-up and an additional 4.5-year extended follow-up. Each dose of 45 to 180 micrograms (mcg) was based on BSA and given as a once-weekly subcutaneous (SC) injection for 48 weeks. BSA-based dosing was as follows: 0.51-0.53 square meters (m^2), 45 mcg; 0.54-0.74 m^2, 65 mcg; 0.75-1.08 m^2, 90 mcg; 1.09-1.51 m^2, 135 mcg; greater than (>) 1.51 m^2, 180 mcg.

Reporting group title	Group B: Untreated Control Without Advanced Fibrosis

Reporting group description:

Participants without advanced fibrosis were randomized and were evaluated for 48 weeks with a 24-week follow-up and an additional ongoing 4.5-year extended follow-up. As the study is open-label, participants did not receive any investigational or placebo treatment during the 48-week principal observation period (POP). For ethical reasons, participants in Group B had a reduced visit schedule (every 12 weeks) compared to participants in Group A through the end of 24-week follow-up. After completing the POP, the same PEG-IFN regimen administered in Group A was offered to participants in Group B who had not experienced hepatitis B envelope antigen (HBeAg) seroconversion. The offer remained for up to 1 year following the Week 48 visit. From the time a given participant switched to PEG-IFN, he/she was no longer included in Group B.

Reporting group title	Group C: PEG-IFN Monotherapy With Advanced Fibrosis

Reporting group description:

Participants with advanced fibrosis were allocated (not randomized) to receive PEG-IFN monotherapy for 48 weeks with a 24-week follow-up and an additional 4.5-year extended follow-up. Each dose of 45 to 180 mcg was based on BSA and given as a once-weekly SC injection for 48 weeks. BSA-based dosing was as follows: 0.51-0.53 m^2, 45 mcg; 0.54-0.74 m^2, 65 mcg; 0.75-1.08 m^2, 90 mcg; 1.09-1.51 m^2, 135 mcg; >1.51 m^2, 180 mcg.

Subject analysis set title	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants without advanced fibrosis were randomized and received PEG-IFN monotherapy for 48 weeks with a 24-week follow-up and an additional 4.5-year extended follow-up. Each dose of 45 to 180 micrograms (mcg) was based on BSA and given as a once-weekly subcutaneous (SC) injection for 48 weeks. BSA-based dosing was as follows: 0.51-0.53 square meters (m^2), 45 mcg; 0.54-0.74 m^2, 65 mcg; 0.75-1.08 m^2, 90 mcg; 1.09-1.51 m^2, 135 mcg; greater than (>) 1.51 m^2, 180 mcg.

Subject analysis set title	Group B: Untreated Control Without Advanced Fibrosis
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants without advanced fibrosis were randomized and were evaluated for 48 weeks with a 24-week follow-up and an additional ongoing 4.5-year extended follow-up. As the study is open-label, participants did not receive any investigational or placebo treatment during the 48-week principal observation period (POP). For ethical reasons, participants in Group B had a reduced visit schedule (every 12 weeks) compared to participants in Group A through the end of 24-week follow-up. After completing the POP, the same PEG-IFN regimen administered in Group A was offered to participants in Group B who had not experienced hepatitis B envelope antigen (HBeAg) seroconversion. The offer remained for up to 1 year following the Week 48 visit. From the time a given participant switched to PEG-IFN, he/she was no longer included in Group B.

Subject analysis set title	Group C: PEG-IFN Monotherapy With Advanced Fibrosis
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants with advanced fibrosis were allocated (not randomized) to receive PEG-IFN monotherapy for 48 weeks with a 24-week follow-up and an additional 4.5-year extended follow-up. Each dose of 45 to 180 mcg was based on BSA and given as a once-weekly SC injection for 48 weeks. BSA-based dosing was as follows: 0.51-0.53 m^2, 45 mcg; 0.54-0.74 m^2, 65 mcg; 0.75-1.08 m^2, 90 mcg; 1.09-1.51 m^2, 135 mcg; >1.51 m^2, 180 mcg.

Subject analysis set title	All Groups Combined
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants without advanced fibrosis were randomized to receive PEG-IFN monotherapy or were evaluated as untreated control for 48 weeks with a 24-week follow-up and an additional ongoing 4.5-year extended follow-up. Participants with advanced fibrosis were allocated (not randomized) to receive PEG-IFN monotherapy for the same duration. For those who received PEG-IFN treatment, each dose of 45 to 180 mcg was based on BSA and given as a once-weekly SC injection for 48 weeks. BSA-based dosing was as follows: 0.51-0.53 m^2, 45 mcg; 0.54-0.74 m^2, 65 mcg; 0.75-1.08 m^2, 90 mcg; 1.09-1.51 m^2, 135 mcg; >1.51 m^2, 180 mcg.

Subject analysis set title	Group D: Switch to PEG-IFN Monotherapy
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants without advanced fibrosis who did not receive treatment and had not experienced HBeAg seroconversion were allowed to switch to PEG-IFN monotherapy. Treatment was given over 48 weeks with a 24-week follow-up and an additional ongoing 4.5-year extended follow-up. Each dose of 45 to 180 mcg was based on BSA and given as a once-weekly SC injection for 48 weeks. BSA-based dosing was as follows: 0.51-0.53 m^2, 45 mcg; 0.54-0.74 m^2, 65 mcg; 0.75-1.08 m^2, 90 mcg; 1.09-1.51 m^2, 135 mcg; >1.51 m^2, 180 mcg.

Primary: Percentage of Participants with HBeAg Seroconversion at 24 Weeks After End of Treatment (EOT)/POP in Groups A and B

End point title	Percentage of Participants with HBeAg Seroconversion at 24 Weeks After End of Treatment (EOT)/POP in Groups A and B[1]

End point description:

HBeAg seroconversion was defined as loss of HBeAg and the presence of hepatitis B envelope antibody (anti-HBe). The percentage of participants with HBeAg seroconversion at 24 weeks after EOT/POP was reported. The 95 percent (%) confidence interval (CI) was calculated by the Pearson-Clopper method. Intent-to-Treat (ITT) Population: All randomized participants regardless of treatment received.

End point type	Primary

End point timeframe:

FU Week 24 (up to 72 weeks overall)

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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	50		
Units: percentage of participants				
number (confidence interval 95%)	25.7 (17.56 to 35.4)	6 (1.25 to 16.55)		

Statistical analyses

Statistical analysis title	Cochran-Mantel-Haenszel

Statistical analysis description:

Analysis stratified by hepatitis B virus (HBV) genotype A versus non-A genotypes and alanine aminotransferase (ALT) less than (<) 5 times (×) upper limit of normal (ULN) versus greater than or equal to (≥) 5 × ULN at Baseline. The OR was calculated using Group B as reference.

Comparison groups	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis v

	Group B: Untreated Control Without Advanced Fibrosis
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0043
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	5.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.54
upper limit	19.2

Statistical analysis title	Breslow-Day
Comparison groups	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis v Group B: Untreated Control Without Advanced Fibrosis
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3732
Method	Breslow-Day

Secondary: Percentage of Participants with Loss of HBeAg at 24 Weeks After EOT/POP in Groups A and B

End point title	Percentage of Participants with Loss of HBeAg at 24 Weeks After EOT/POP in Groups A and B[2]

End point description:

The percentage of participants with loss of HBeAg at 24 weeks after EOT/POP was reported. The 95% CI was calculated by the Pearson-Clopper method. ITT Population.

End point type	Secondary

End point timeframe:

FU Week 24 (up to 72 weeks overall)

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	50		
Units: percentage of participants				
number (confidence interval 95%)	25.7 (17.56 to	6 (1.25 to		

35.4)	16.55)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Hepatitis B Surface Antigen (HBsAg) Seroconversion at 24 Weeks After EOT/POP in Groups A and B

End point title	Percentage of Participants with Hepatitis B Surface Antigen (HBsAg) Seroconversion at 24 Weeks After EOT/POP in Groups A and B[3]

End point description:

HBsAg seroconversion was defined as loss of HBsAg and the presence of hepatitis B surface antibody (anti-HBs). The percentage of participants with HBsAg seroconversion at 24 weeks after EOT/POP was reported. The 95% CI was calculated by the Pearson-Clopper method. ITT Population.

End point type	Secondary

End point timeframe:

FU Week 24 (up to 72 weeks overall)

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	50		
Units: percentage of participants				
number (confidence interval 95%)	7.9 (3.48 to 15.01)	0 (0 to 7.11)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Normal ALT at 24 Weeks After EOT/POP in Groups A and B

End point title	Percentage of Participants with Normal ALT at 24 Weeks After EOT/POP in Groups A and B[4]

End point description:

Normal ALT was defined as ALT less than or equal to (≤) ULN, where each ULN was given by the laboratory at which the sample was analyzed. The percentage of participants with normal ALT at 24 weeks after EOT/POP was reported. The 95% CI was calculated by the Pearson-Clopper method. ITT Population.

End point type	Secondary

End point timeframe:

FU Week 24 (up to 72 weeks overall)

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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	50		
Units: percentage of participants				
number (confidence interval 95%)	51.5 (41.33 to 61.55)	12 (4.53 to 24.31)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HBV Deoxyribonucleic Acid (DNA) <20,000 International Units per Milliliter (IU/mL) at 24 Weeks After EOT/POP in Groups A and B

End point title	Percentage of Participants with HBV Deoxyribonucleic Acid (DNA) <20,000 International Units per Milliliter (IU/mL) at 24 Weeks After EOT/POP in Groups A and B[5]

End point description:

HBV DNA was quantified using polymerase chain reaction (PCR) by Roche Taqman. The percentage of participants with HBV DNA <20,000 IU/mL at 24 weeks after EOT/POP was reported. The 95% CI was calculated by the Pearson-Clopper method. ITT Population.

End point type	Secondary

End point timeframe:

FU Week 24 (up to 72 weeks overall)

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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	50		
Units: percentage of participants				
number (confidence interval 95%)	33.7 (24.56 to	4 (0.49 to		

43.75)	13.71)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HBV DNA <2,000 IU/mL at 24 Weeks After EOT/POP in Groups A and B

End point title	Percentage of Participants with HBV DNA <2,000 IU/mL at 24 Weeks After EOT/POP in Groups A and B[6]

End point description:

HBV DNA was quantified using PCR by Roche Taqman. The percentage of participants with HBV DNA <2,000 IU/mL at 24 weeks after EOT/POP was reported. The 95% CI was calculated by the Pearson-Clopper method. ITT Population.

End point type	Secondary

End point timeframe:

FU Week 24 (up to 72 weeks overall)

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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	50		
Units: percentage of participants				
number (confidence interval 95%)	28.7 (20.15 to 38.57)	2 (0.05 to 10.65)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Combined HBeAg Seroconversion and HBV DNA <20,000 IU/mL at 24 Weeks After EOT/POP in Groups A and B

End point title	Percentage of Participants with Combined HBeAg Seroconversion and HBV DNA <20,000 IU/mL at 24 Weeks After EOT/POP in Groups A and B[7]

End point description:

HBeAg seroconversion was defined as loss of HBeAg and the presence of anti-HBe. HBV DNA was quantified using PCR by Roche Taqman. The percentage of participants with combined HBeAg seroconversion and HBV DNA <20,000 IU/mL at 24 weeks after EOT/POP was reported. The 95% CI was calculated by the Pearson-Clopper method. ITT Population.

End point type	Secondary

End point timeframe:

FU Week 24 (up to 72 weeks overall)

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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	50		
Units: percentage of participants				
number (confidence interval 95%)	22.8 (15.02 to 32.18)	4 (0.49 to 13.71)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Combined HBeAg Seroconversion and HBV DNA <2,000 IU/mL at 24 Weeks After EOT/POP in Groups A and B

End point title	Percentage of Participants with Combined HBeAg Seroconversion and HBV DNA <2,000 IU/mL at 24 Weeks After EOT/POP in Groups A and B[8]

End point description:

HBeAg seroconversion was defined as loss of HBeAg and the presence of anti-HBe. HBV DNA was quantified using PCR by Roche Taqman. The percentage of participants with combined HBeAg seroconversion and HBV DNA <2,000 IU/mL at 24 weeks after EOT/POP was reported. The 95% CI was calculated by the Pearson-Clopper method. ITT Population.

End point type	Secondary

End point timeframe:

FU Week 24 (up to 72 weeks overall)

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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	50		
Units: percentage of participants				
number (confidence interval 95%)	19.8 (12.54 to	2 (0.05 to		

28.91)	10.65)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HBeAg Seroconversion at EOT/POP in Groups A and B

End point title	Percentage of Participants with HBeAg Seroconversion at EOT/POP in Groups A and B[9]

End point description:

HBeAg seroconversion was defined as loss of HBeAg and the presence of anti-HBe. The percentage of participants with HBeAg seroconversion at EOT/POP was reported. The 95% CI was calculated by the Pearson-Clopper method. ITT Population.

End point type	Secondary

End point timeframe:

Week 48

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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	50		
Units: percentage of participants				
number (confidence interval 95%)	7.9 (3.48 to 15.01)	6 (1.25 to 16.55)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Loss of HBeAg at EOT/POP in Groups A and B

End point title	Percentage of Participants with Loss of HBeAg at EOT/POP in Groups A and B[10]

End point description:

The percentage of participants with loss of HBeAg at EOT/POP was reported. The 95% CI was calculated by the Pearson-Clopper method. ITT Population.

End point type	Secondary

End point timeframe:

Week 48

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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	50		
Units: percentage of participants				
number (confidence interval 95%)	8.9 (4.16 to 16.24)	6 (1.25 to 16.55)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HBsAg Seroconversion at EOT/POP in Groups A and B

End point title	Percentage of Participants with HBsAg Seroconversion at EOT/POP in Groups A and B[11]

End point description:

HBsAg seroconversion was defined as loss of HBsAg and the presence of anti-HBs. The percentage of participants with HBsAg seroconversion at EOT/POP was reported. The 95% CI was calculated by the Pearson-Clopper method. ITT Population.

End point type	Secondary

End point timeframe:

Week 48

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	50		
Units: percentage of participants				
number (confidence interval 95%)	6.9 (2.83 to 13.76)	0 (0 to 7.11)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Loss of HBsAg at EOT/POP in Groups A and B

End point title	Percentage of Participants with Loss of HBsAg at EOT/POP in Groups A and B[12]

End point description:

The percentage of participants with loss of HBsAg at EOT/POP was reported. The 95% CI was calculated by the Pearson-Clopper method. ITT Population.

End point type	Secondary

End point timeframe:

Week 48

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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	50		
Units: percentage of participants				
number (confidence interval 95%)	10.9 (5.56 to 18.65)	0 (0 to 7.11)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Normal ALT at EOT/POP in Groups A and B

End point title	Percentage of Participants with Normal ALT at EOT/POP in Groups A and B[13]

End point description:

Normal ALT was defined as ALT ≤ ULN, where each ULN was given by the laboratory at which the sample was analyzed. The percentage of participants with normal ALT at EOT/POP was reported. The 95% CI was calculated by the Pearson-Clopper method. ITT Population.

End point type	Secondary

End point timeframe:

Week 48

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	50		
Units: percentage of participants				
number (confidence interval 95%)	18.8 (11.72 to 27.81)	22 (11.53 to 35.96)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HBV DNA <20,000 IU/mL at EOT/POP in Groups A and B

End point title	Percentage of Participants with HBV DNA <20,000 IU/mL at EOT/POP in Groups A and B[14]

End point description:

HBV DNA was quantified using PCR by Roche Taqman. The percentage of participants with HBV DNA <20,000 IU/mL at EOT/POP was reported. The 95% CI was calculated by the Pearson-Clopper method. ITT Population.

End point type	Secondary

End point timeframe:

Week 48

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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	50		
Units: percentage of participants				
number (confidence interval 95%)	36.6 (27.27 to 46.81)	12 (4.53 to 24.31)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HBV DNA <2,000 IU/mL at EOT/POP in Groups A and B

End point title	Percentage of Participants with HBV DNA <2,000 IU/mL at EOT/POP in Groups A and B[15]

End point description:

HBV DNA was quantified using PCR by Roche Taqman. The percentage of participants with HBV DNA <2,000 IU/mL at EOT/POP was reported. The 95% CI was calculated by the Pearson-Clopper method. ITT Population.

End point type	Secondary

End point timeframe:

Week 48

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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	50		
Units: percentage of participants				
number (confidence interval 95%)	30.7 (21.9 to 40.66)	2 (0.05 to 10.65)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HBV DNA Undetectable at EOT/POP in Groups A and B

End point title	Percentage of Participants with HBV DNA Undetectable at EOT/POP in Groups A and B[16]

End point description:

HBV DNA was quantified using PCR by Roche Taqman. Undetectable HBV DNA was defined as HBV DNA <29 IU/mL. The percentage of participants with HBV DNA undetectable at EOT/POP was reported. The 95% CI was calculated by the Pearson-Clopper method. ITT Population.

End point type	Secondary

End point timeframe:

Week 48

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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	50		
Units: percentage of participants				
number (confidence interval 95%)	18.8 (11.72 to 27.81)	0 (0 to 7.11)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Combined HBeAg Seroconversion and HBV DNA <20,000 IU/mL at EOT/POP in Groups A and B

End point title	Percentage of Participants with Combined HBeAg Seroconversion and HBV DNA <20,000 IU/mL at EOT/POP in Groups A and B[17]

End point description:

HBeAg seroconversion was defined as loss of HBeAg and the presence of anti-HBe. HBV DNA was quantified using PCR by Roche Taqman. The percentage of participants with combined HBeAg seroconversion and HBV DNA <20,000 IU/mL at EOT/POP was reported. The 95% CI was calculated by the Pearson-Clopper method. ITT Population.

End point type	Secondary

End point timeframe:

Week 48

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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	50		
Units: percentage of participants				
number (confidence interval 95%)	6.9 (2.83 to	6 (1.25 to		

13.76)	16.55)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Combined HBeAg Seroconversion and HBV DNA <2,000 IU/mL at EOT/POP in Groups A and B

End point title	Percentage of Participants with Combined HBeAg Seroconversion and HBV DNA <2,000 IU/mL at EOT/POP in Groups A and B[18]

End point description:

HBeAg seroconversion was defined as loss of HBeAg and the presence of anti-HBe. HBV DNA was quantified using PCR by Roche Taqman. The percentage of participants with combined HBeAg seroconversion and HBV DNA <2,000 IU/mL at EOT/POP was reported. The 95% CI was calculated by the Pearson-Clopper method. ITT Population.

End point type	Secondary

End point timeframe:

Week 48

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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	50		
Units: percentage of participants				
number (confidence interval 95%)	6.9 (2.83 to 13.76)	0 (0 to 7.11)		

Statistical analyses

No statistical analyses for this end point

Secondary: Quantitative Serum ALT Level in Groups A and B

End point title	Quantitative Serum ALT Level in Groups A and B[19]

End point description:

Quantitative ALT at each visit was averaged among all participants and expressed as a factor of the laboratory-specific ULN (for example, 1 × ULN, 2 × ULN, 3 × ULN). ITT Population. The number of participants who provided evaluable data for the analysis at each timepoint (n) is shown in the table. Values entered as "99999" mean that the calculation was not performed because no participants

provided data for the visit.

End point type	Secondary

End point timeframe:

Baseline; Weeks 1, 2, 4, 8, 12, 18, 24, 30, 36, 42, 48; FU Weeks 4, 12, 24 (up to 72 weeks overall)

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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	50		
Units: factor of ULN				
arithmetic mean (standard deviation)				
Baseline (n=101,50)	2.779 (± 2.483)	2.878 (± 1.997)		
Week 1 (n=98,0)	3.427 (± 2.687)	99999 (± 99999)		
Week 2 (n=99,0)	2.846 (± 1.885)	99999 (± 99999)		
Week 4 (n=101,0	3.343 (± 2.455)	99999 (± 99999)		
Week 8 (n=100,0)	3.262 (± 2.797)	99999 (± 99999)		
Week 12 (n=97,49)	3.189 (± 3.06)	3.492 (± 6.532)		
Week 18 (n=98,0)	3.036 (± 2.389)	99999 (± 99999)		
Week 24 (n=99,47)	2.753 (± 2.725)	2.401 (± 2.638)		
Week 30 (n=98,0)	2.587 (± 2.128)	99999 (± 99999)		
Week 36 (n=99,47)	2.45 (± 1.856)	2.341 (± 2.204)		
Week 42 (n=99,0)	2.316 (± 1.429)	99999 (± 99999)		
Week 48 (n=99,46)	2.122 (± 1.389)	1.954 (± 1.371)		
FU Week 4 (n=99,0)	1.303 (± 1.74)	99999 (± 99999)		
FU Week 12 (n=100,0)	2.064 (± 2.027)	99999 (± 99999)		
FU Week 24 (n=101,15)	1.477 (± 1.625)	1.7 (± 1.385)		

Statistical analyses

No statistical analyses for this end point

Secondary: Quantitative HBV DNA Level in Groups A and B

End point title	Quantitative HBV DNA Level in Groups A and B[20]

End point description:

Quantitative HBV DNA at each visit was averaged among all participants and expressed in log10 IU/mL. ITT Population. The number of participants who provided evaluable data for the analysis at each timepoint (n) is shown in the table. Values entered as "99999" mean that the calculation was not performed because no participants provided data for the visit.

End point type	Secondary

End point timeframe:

Baseline; Weeks 12, 24, 36, 48; FU Weeks 4, 12, 24 (up to 72 weeks overall)

Notes:

[20] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	50		
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Baseline (n=101,50)	8.094 (± 0.986)	8.056 (± 0.987)		
Week 12 (n=98,49)	6.49 (± 2.009)	7.909 (± 1.267)		
Week 24 (n=99,46)	5.966 (± 2.398)	7.857 (± 1.327)		
Week 36 (n=99,47)	5.575 (± 2.513)	7.685 (± 1.608)		
Week 48 (n=99,47)	5.224 (± 2.701)	7.551 (± 1.761)		
FU Week 4 (n=97,0)	5.739 (± 2.935)	99999 (± 99999)		
FU Week 12 (n=98,21)	5.914 (± 3.065)	7.214 (± 2.46)		
FU Week 24 (n=98,13)	5.707 (± 3.113)	7.2 (± 2.506)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Quantitative HBV DNA Level in Groups A and B

End point title	Change from Baseline in Quantitative HBV DNA Level in Groups A and B[21]

End point description:

The change in quantitative HBV DNA from Baseline to each visit was averaged among all participants and expressed in log10 IU/mL. ITT Population. All participants were included in the endpoint analysis. The number of participants who provided evaluable data for the analysis at each timepoint (n) is shown

in the table. Values entered as "99999" mean that the calculation was not performed because no participants provided data for the visit.

End point type	Secondary

End point timeframe:

Weeks 12, 24, 36, 48; FU Weeks 4, 12, 24 (up to 72 weeks overall)

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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	50		
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Week 12 (n=98,49)	-1.588 (± 1.625)	-0.156 (± 1.093)		
Week 24 (n=99,46)	-2.112 (± 1.996)	-0.168 (± 1.214)		
Week 36 (n=99,47)	-2.525 (± 2.148)	-0.359 (± 1.411)		
Week 48 (n=99,47)	-2.877 (± 2.374)	-0.493 (± 1.518)		
FU Week 4 (n=97,0)	-2.34 (± 2.582)	99999 (± 99999)		
FU Week 12 (n=98,21)	-2.164 (± 2.737)	-0.86 (± 2.163)		
FU Week 24 (n=98,13)	-2.381 (± 2.778)	-0.587 (± 2.259)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Loss of HBeAg at 24 Weeks After EOT in Group C

End point title	Percentage of Participants with Loss of HBeAg at 24 Weeks After EOT in Group C[22]

End point description:

The percentage of participants with loss of HBeAg at 24 weeks after EOT was reported. The 95% CI was calculated by the Pearson-Clopper method. Safety Population: All participants who received at least one dose of study drug (if assigned) and had at least one post-baseline safety assessment.

End point type	Secondary

End point timeframe:

FU Week 24 (up to 72 weeks overall)

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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of participants				
number (confidence interval 95%)	30 (6.67 to 65.25)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Loss of HBsAg at 24 Weeks After EOT in Group C

End point title	Percentage of Participants with Loss of HBsAg at 24 Weeks After EOT in Group C[23]

End point description:

The percentage of participants with loss of HBsAg at 24 weeks after EOT was reported. The 95% CI was calculated by the Pearson-Clopper method. Safety Population

End point type	Secondary

End point timeframe:

FU Week 24 (up to 72 weeks overall)

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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of participants				
arithmetic mean (confidence interval 95%)	0 (0 to 30.85)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HBsAg Seroconversion at 24 Weeks After EOT in Group C

End point title	Percentage of Participants with HBsAg Seroconversion at 24 Weeks After EOT in Group C[24]

End point description:

HBsAg seroconversion was defined as loss of HBsAg and the presence of anti-HBs. The percentage of participants with HBsAg seroconversion at 24 weeks after EOT was reported. The 95% CI was calculated by the Pearson-Clopper method. Safety Population.

End point type	Secondary

End point timeframe:

FU Week 24 (up to 72 weeks overall)

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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of participants				
number (confidence interval 95%)	0 (0 to 30.85)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Normal ALT at 24 Weeks After EOT in Group C

End point title	Percentage of Participants with Normal ALT at 24 Weeks After EOT in Group C[25]

End point description:

Normal ALT was defined as ALT ≤ ULN, where each ULN was given by the laboratory at which the sample was analyzed. The percentage of participants with normal ALT at 24 weeks after EOT was reported. The 95% CI was calculated by the Pearson-Clopper method. Safety Population.

End point type	Secondary

End point timeframe:

FU Week 24 (up to 72 weeks overall)

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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of participants				
number (confidence interval 95%)	70 (34.75 to 93.33)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HBV DNA <2,000 IU/mL at 24 Weeks After EOT in Group C

End point title	Percentage of Participants with HBV DNA <2,000 IU/mL at 24 Weeks After EOT in Group C[26]

End point description:

HBV DNA was quantified using PCR by Roche Taqman. The percentage of participants with HBV DNA <2,000 IU/mL at 24 weeks after EOT was reported. The 95% CI was calculated by the Pearson-Clopper method. Safety Population.

End point type	Secondary

End point timeframe:

FU Week 24 (up to 72 weeks overall)

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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of participants				
number (confidence interval 95%)	70 (34.75 to 93.33)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HBV DNA <20,000 IU/mL at 24 Weeks After EOT in Group C

End point title	Percentage of Participants with HBV DNA <20,000 IU/mL at 24

	Weeks After EOT in Group C[27]

End point description:

HBV DNA was quantified using PCR by Roche Taqman. The percentage of participants with HBV DNA <20,000 IU/mL at 24 weeks after EOT was reported. The 95% CI was calculated by the Pearson-Clopper method. Safety Population.

End point type	Secondary

End point timeframe:

FU Week 24 (up to 72 weeks overall)

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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of participants				
number (confidence interval 95%)	70 (34.75 to 93.33)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HBV DNA Undetectable at 24 Weeks After EOT in Group C

End point title	Percentage of Participants with HBV DNA Undetectable at 24 Weeks After EOT in Group C[28]

End point description:

HBV DNA was quantified using PCR by Roche Taqman. Undetectable HBV DNA was defined as HBV DNA <29 IU/mL. The percentage of participants with HBV DNA undetectable at 24 weeks after EOT was reported. The 95% CI was calculated by the Pearson-Clopper method. Safety Population.

End point type	Secondary

End point timeframe:

FU Week 24 (up to 72 weeks overall)

Notes:

[28] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of participants				
number (confidence interval 95%)	30 (6.67 to 65.25)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Combined HBeAg Seroconversion and HBV DNA <20,000 IU/mL at 24 Weeks After EOT in Group C

End point title	Percentage of Participants with Combined HBeAg Seroconversion and HBV DNA <20,000 IU/mL at 24 Weeks After EOT in Group C[29]

End point description:

HBeAg seroconversion was defined as loss of HBeAg and the presence of anti-HBe. HBV DNA was quantified using PCR by Roche Taqman. The percentage of participants with combined HBeAg seroconversion and HBV DNA <20,000 IU/mL at 24 weeks after EOT was reported. The 95% CI was calculated by the Pearson-Clopper method. Safety Population.

End point type	Secondary

End point timeframe:

FU Week 24 (up to 72 weeks overall)

Notes:

[29] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of participants				
number (confidence interval 95%)	30 (6.67 to 65.25)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Combined HBeAg Seroconversion and HBV DNA <2,000 IU/mL at 24 Weeks After EOT in Group C

End point title	Percentage of Participants with Combined HBeAg Seroconversion and HBV DNA <2,000 IU/mL at 24 Weeks After EOT in Group C[30]

End point description:

HBeAg seroconversion was defined as loss of HBeAg and the presence of anti-HBe. HBV DNA was quantified using PCR by Roche Taqman. The percentage of participants with combined HBeAg seroconversion and HBV DNA <2,000 IU/mL at 24 weeks after EOT was reported. The 95% CI was calculated by the Pearson-Clopper method. Safety Population.

End point type	Secondary

End point timeframe:

FU Week 24 (up to 72 weeks overall)

Notes:

[30] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of participants				
number (confidence interval 95%)	30 (6.67 to 65.25)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Loss of HBeAg at EOT in Group C

End point title	Percentage of Participants with Loss of HBeAg at EOT in Group C[31]

End point description:

The percentage of participants with loss of HBeAg at EOT was reported. The 95% CI was calculated by the Pearson-Clopper method. Safety Population.

End point type	Secondary

End point timeframe:

Week 48

Notes:

[31] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of participants				
number (confidence interval 95%)	20 (2.52 to 55.61)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HBeAg Seroconversion at EOT in Group C

End point title	Percentage of Participants with HBeAg Seroconversion at EOT in Group C[32]

End point description:

HBeAg seroconversion was defined as loss of HBeAg and the presence of anti-HBe. The percentage of participants with HBeAg seroconversion at EOT was reported. The 95% CI was calculated by the Pearson-Clopper method. Safety Population.

End point type	Secondary

End point timeframe:

Week 48

Notes:

[32] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of participants				
number (confidence interval 95%)	20 (2.52 to 55.61)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HBsAg Seroconversion at EOT in Group C

End point title	Percentage of Participants with HBsAg Seroconversion at EOT in Group C[33]

End point description:

HBsAg seroconversion was defined as loss of HBsAg and the presence of anti-HBs. The percentage of participants with HBsAg seroconversion at EOT was reported. The 95% CI was calculated by the Pearson-Clopper method. Safety Population.

End point type	Secondary

End point timeframe:

Week 48

Notes:

[33] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of participants				
number (confidence interval 95%)	0 (0 to 30.85)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Normal ALT at EOT in Group C

End point title	Percentage of Participants with Normal ALT at EOT in Group

End point description:

Normal ALT was defined as ALT ≤ ULN, where each ULN was given by the laboratory at which the sample was analyzed. The percentage of participants with normal ALT at EOT was reported. The 95% CI was calculated by the Pearson-Clopper method. Safety Population.

End point type	Secondary

End point timeframe:

Week 48

Notes:

[34] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of participants				
number (confidence interval 95%)	40 (12.16 to			

	73.76)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Loss of HBsAg at EOT in Group C

End point title	Percentage of Participants with Loss of HBsAg at EOT in Group C[35]

End point description:

The percentage of participants with loss of HBsAg at EOT was reported. The 95% CI was calculated by the Pearson-Clopper method. Safety Population.

End point type	Secondary

End point timeframe:

Week 48

Notes:

[35] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of participants				
number (confidence interval 95%)	0 (0 to 30.85)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HBV DNA <20,000 IU/mL at EOT in Group C

End point title	Percentage of Participants with HBV DNA <20,000 IU/mL at EOT in Group C[36]

End point description:

HBV DNA was quantified using PCR by Roche Taqman. The percentage of participants with HBV DNA <20,000 IU/mL at EOT was reported. The 95% CI was calculated by the Pearson-Clopper method. Safety Population.

End point type	Secondary

End point timeframe:

Week 48

Notes:

[36] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of participants				
number (confidence interval 95%)	40 (12.16 to 73.76)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HBV DNA <2,000 IU/mL at EOT in Group C

End point title	Percentage of Participants with HBV DNA <2,000 IU/mL at EOT in Group C[37]

End point description:

HBV DNA was quantified using PCR by Roche Taqman. The percentage of participants with HBV DNA <2,000 IU/mL at EOT was reported. The 95% CI was calculated by the Pearson-Clopper method. Safety Population.

End point type	Secondary

End point timeframe:

Week 48

Notes:

[37] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of participants				
number (confidence interval 95%)	30 (6.67 to 65.25)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HBV DNA Undetectable at EOT in Group C

End point title	Percentage of Participants with HBV DNA Undetectable at EOT in Group C[38]

End point description:

HBV DNA was quantified using PCR by Roche Taqman. Undetectable HBV DNA was defined as HBV DNA <29 IU/mL. The percentage of participants with HBV DNA undetectable at EOT was reported. The 95% CI was calculated by the Pearson-Clopper method. Safety Population.

End point type	Secondary

End point timeframe:

Week 48

Notes:

[38] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of participants				
number (confidence interval 95%)	20 (2.52 to 55.61)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Combined HBeAg Seroconversion and HBV DNA <20,000 IU/mL at EOT in Group C

End point title	Percentage of Participants with Combined HBeAg Seroconversion and HBV DNA <20,000 IU/mL at EOT in Group C[39]

End point description:

HBeAg seroconversion was defined as loss of HBeAg and the presence of anti-HBe. HBV DNA was quantified using PCR by Roche Taqman. The percentage of participants with combined HBeAg seroconversion and HBV DNA <20,000 IU/mL at EOT was reported. The 95% CI was calculated by the Pearson-Clopper method. Safety Population.

End point type	Secondary

End point timeframe:

Week 48

Notes:

[39] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried

out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of participants				
number (confidence interval 95%)	20 (2.52 to 55.61)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Combined HBeAg Seroconversion and HBV DNA <2,000 IU/mL at EOT in Group C

End point title	Percentage of Participants with Combined HBeAg Seroconversion and HBV DNA <2,000 IU/mL at EOT in Group C[40]

End point description:

HBeAg seroconversion was defined as loss of HBeAg and the presence of anti-HBe. HBV DNA was quantified using PCR by Roche Taqman. The percentage of participants with combined HBeAg seroconversion and HBV DNA <2,000 IU/mL at EOT was reported. The 95% CI was calculated by the Pearson-Clopper method. Safety Population.

End point type	Secondary

End point timeframe:

Week 48

Notes:

[40] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of participants				
number (confidence interval 95%)	20 (2.52 to 55.61)			

Statistical analyses

No statistical analyses for this end point

Secondary: Quantitative Serum ALT Level in Group C

End point title	Quantitative Serum ALT Level in Group C[41]

End point description:

Quantitative ALT at each visit was averaged among all participants and expressed as a factor of the laboratory-specific ULN (for example, 1 × ULN, 2 × ULN, 3 × ULN). Safety Population. The number of participants who provided evaluable data for the analysis at each timepoint (n) is shown in the table.

End point type	Secondary

End point timeframe:

Baseline; Weeks 1, 2, 4, 8, 12, 18, 24, 30, 36, 42, 48; FU Weeks 4, 12, 24 (up to 72 weeks overall)

Notes:

[41] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: factor of ULN				
arithmetic mean (standard deviation)				
Baseline (n=10)	2.804 (± 1.118)			
Week 1 (n=10)	3.117 (± 1.322)			
Week 2 (n=10)	2.896 (± 1.304)			
Week 4 (n=10)	2.444 (± 1.727)			
Week 8 (n=10)	2.703 (± 2.035)			
Week 12 (n=10)	2.793 (± 1.288)			
Week 18 (n=10)	2.215 (± 1.032)			
Week 24 (n=10)	1.887 (± 1.095)			
Week 30 (n=10)	2.22 (± 1.553)			
Week 36 (n=10)	2.172 (± 1.09)			
Week 42 (n=10)	1.593 (± 0.516)			
Week 48 (n=9)	1.645 (± 1.242)			
FU Week 4 (n=10)	1.136 (± 0.506)			
FU Week 12 (n=10)	1.521 (± 0.755)			
FU Week 24 (n=10)	1.549 (± 1.595)			

Statistical analyses

No statistical analyses for this end point

Secondary: Quantitative HBV DNA Level in Group C

End point title	Quantitative HBV DNA Level in Group C[42]

End point description:

Quantitative HBV DNA at each visit was averaged among all participants and expressed in log10 IU/mL. Safety Population. The number of participants who provided evaluable data for the analysis at each timepoint (n) is shown in the table.

End point type	Secondary

End point timeframe:

Baseline; Weeks 12, 24, 36, 48; FU Weeks 4, 12, 24 (up to 72 weeks overall)

Notes:

[42] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Baseline (n=10)	7.866 (± 0.977)			
Week 12 (n=10)	5.782 (± 1.771)			
Week 24 (n=10)	5.599 (± 2.386)			
Week 36 (n=9)	5.2 (± 2.451)			
Week 48 (n=10)	5.319 (± 2.747)			
FU Week 4 (n=10)	4.604 (± 2.442)			
FU Week 12 (n=10)	4.252 (± 2.596)			
FU Week 24 (n=9)	3.694 (± 3.127)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Quantitative HBV DNA Level in Group C

End point title	Change from Baseline in Quantitative HBV DNA Level in Group C[43]

End point description:

The change in quantitative HBV DNA from Baseline to each visit was averaged among all participants and expressed in log10 IU/mL. Safety Population. The number of participants who provided evaluable data for the analysis at each timepoint (n) is shown in the table.

End point type	Secondary

End point timeframe:

Weeks 12, 24, 36, 48; FU Weeks 4, 12, 24 (up to 72 weeks overall)

Notes:

[43] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Week 12 (n=10)	-2.084 (± 1.1)			
Week 24 (n=10)	-2.267 (± 1.595)			
Week 36 (n=9)	-2.529 (± 1.879)			
Week 48 (n=10)	-2.546 (± 2.14)			
FU Week 4 (n=10)	-3.262 (± 2.102)			
FU Week 12 (n=10)	-3.613 (± 2.519)			
FU Week 24 (n=9)	-4.15 (± 2.904)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Liver Stiffness Measure (LSM) in Groups A, B, C

End point title	Change from Baseline in Liver Stiffness Measure (LSM) in Groups A, B, C

End point description:

Liver elastography was performed to assess elasticity and extent of hepatic fibrosis. The change in LSM from Baseline to each visit was averaged among all participants in expressed in kilopascals (kPa). Positive changes in LSM values corresponded to an increase in stiffness and hepatic fibrosis. Liver Substudy Population: All participants who consented to participate in the liver elasticity substudy.

"Number of subjects analyzed" reflects the total number of participants who provided evaluable data at any timepoint. The number of participants who provided evaluable data for the analysis at each timepoint (n) is shown in the table.

End point type	Secondary

End point timeframe:

Week 48; FU Week 24 (up to 72 weeks overall)

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis	Group C: PEG-IFN Monotherapy With Advanced Fibrosis	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	44	25	6	
Units: kPa				
arithmetic mean (standard deviation)				
Week 48 (n=40,21,6)	-0.49 (± 2.151)	0.376 (± 2.719)	-1.517 (± 1.685)	
FU Week 24 (n=38,5,6)	-1.026 (± 2.269)	-0.72 (± 2.633)	-1.7 (± 1.033)	

Statistical analyses

No statistical analyses for this end point

Secondary: Estimated Area Under the Concentration-Time Curve (AUC) by BSA Category

End point title	Estimated Area Under the Concentration-Time Curve (AUC) by BSA Category

End point description:

AUC was estimated using population pharmacokinetic (PK) modeling. The AUC at steady-state was averaged among participants who received PEG-IFN and reported by BSA category. Categories of BSA-based dosing used in the analysis were as follows: 0.54-0.74 m^2, 65 mcg; 0.75-1.08 m^2, 90 mcg; 1.09-1.51 m^2, 135 mcg; >1.51 m^2, 180 mcg. The estimated AUC was expressed in hours by nanograms per milliliter (h*ng/mL). PK Substudy Population: All participants who consented to participate in the PK substudy. "Number of subjects analyzed" reflects the total combined number of participants who provided evaluable data across all BSA categories. The number of participants who provided evaluable data within each BSA category (n) is shown in the table.

End point type	Secondary

End point timeframe:

Pre-dose (0 hours) at Baseline and Weeks 4, 8, 12, 24; post-dose (24-48, 72-96, 168 hours) during Weeks 1, 24 (up to 24 weeks overall)

End point values	All Groups Combined			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: h*ng/mL				
arithmetic mean (full range (min-max))				
0.54–0.74 m^2 (n=5)	3320 (633 to 5064)			
0.75–1.08 m^2 (n=11)	4037 (1897 to 6916)			
1.09–1.51 m^2 (n=7)	2765 (1750 to 4392)			
>1.51 m^2 (n=7)	3448 (1914 to 5000)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with >15% Drop in Height Percentile for Age in Groups A and B

End point title	Percentage of Participants with >15% Drop in Height Percentile for Age in Groups A and B[44]

End point description:

The percentage of participants with >15% drop in height percentile for age from Baseline to each visit was reported. Safety Population. "Number of subjects analyzed" reflects the total number of participants who provided evaluable data at any timepoint. The number of participants who provided evaluable data for the analysis at each timepoint (n) is shown in the table.

End point type	Secondary

End point timeframe:

Weeks 12, 24, 36, 48; FU Weeks 12, 24 (up to 72 weeks overall)

Notes:

[44] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	48		
Units: percentage of participants				
number (not applicable)				
Week 12 (n=99,48)	1	0		
Week 24 (n=100,47)	5	8.5		
Week 36 (n=99,48)	4	4.2		
Week 48 (n=98,47)	6.1	2.1		
FU Week 12 (n=101,24)	10.9	4.2		
FU Week 24 (n=100,15)	12	6.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with >15% Drop in Weight Percentile for Age in Groups A and B

End point title	Percentage of Participants with >15% Drop in Weight Percentile for Age in Groups A and B[45]

End point description:

The percentage of participants with >15% drop in weight percentile for age from Baseline to each visit was reported. Safety Population. "Number of subjects analyzed" reflects the total number of participants who provided evaluable data at any timepoint. The number of participants who provided evaluable data for the analysis at each timepoint (n) is shown in the table. Values entered as "99999" mean that the calculation was not performed because no participants provided data for the visit.

End point type	Secondary

End point timeframe:

Weeks 4, 8, 12, 18, 24, 30, 36, 42, 48; FU Weeks 4, 12, 24 (up to 72 weeks overall)

Notes:

[45] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	48		
Units: percentage of participants				
number (not applicable)				
Week 4 (n=101,0)	2	99999		
Week 8 (n=101,0)	5	99999		
Week 12 (n=99,48)	5.1	2.1		
Week 18 (n=99,0)	8.1	99999		
Week 24 (n=100,47)	16	8.5		
Week 30 (n=99,0)	13.1	99999		
Week 36 (n=97,48)	11.3	8.3		
Week 42 (n=99,0)	13.1	99999		
Week 48 (n=96,47)	12.5	8.5		
FU Week 4 (n=99,0)	8.1	99999		
FU Week 12 (n=101,24)	6.9	20.8		
FU Week 24 (n=100,15)	11	20		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with >15% Drop in Height Percentile for Age in Group C

End point title	Percentage of Participants with >15% Drop in Height Percentile for Age in Group C[46]

End point description:

The percentage of participants with >15% drop in weight percentile for age from Baseline to each visit was reported. Safety Population.

End point type	Secondary

End point timeframe:

Weeks 30, 36; FU Weeks 4, 12, 24 (up to 72 weeks overall)

Notes:

[46] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of participants				
number (not applicable)				
Week 30	20			
Week 36	10			
FU Week 4	10			
FU Week 12	10			
FU Week 24	20			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Height for Age Z-Score in Groups A and B

End point title	Change From Baseline in Height for Age Z-Score in Groups A and B[47]

End point description:

The difference between the population mean and raw scores was calculated as the height for age z-

score. Mean absolute values at Baseline were reported. The change from Baseline to each visit was averaged among all participants and expressed in units of standard deviations. Safety Population. "Number of subjects analyzed" reflects the total number of participants who provided evaluable data at any timepoint. The number of participants who provided evaluable data for the analysis at each timepoint (n) is shown in the table.

End point type	Secondary

End point timeframe:

Baseline; Weeks 12, 24, 36, 48; FU Weeks 12, 24 (up to 72 weeks overall)

Notes:

[47] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	49		
Units: standard deviations				
arithmetic mean (standard deviation)				
Baseline (n=101,49)	0.271 (± 1.149)	-0.062 (± 1.17)		
Week 12 (n=99,48	0.011 (± 0.258)	-0.006 (± 0.185)		
Week 24 (n=100,47)	-0.04 (± 0.293)	-0.071 (± 0.264)		
Week 36 (n=99,48)	-0.056 (± 0.337)	-0.025 (± 0.328)		
Week 48 (n=98,47)	-0.099 (± 0.365)	-0.013 (± 0.284)		
FU Week 12 (n=101,24)	-0.112 (± 0.404)	-0.037 (± 0.243)		
FU Week 24 (n=100,15)	-0.117 (± 0.429)	-0.079 (± 0.282)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Weight for Age Z-Score in Groups A and B

End point title	Change From Baseline in Weight for Age Z-Score in Groups A and B[48]

End point description:

The difference between the population mean and raw scores was calculated as the weight for age z-score. Mean absolute values at Baseline were reported. The change from Baseline to each visit was averaged among all participants and expressed in units of standard deviations.Safety Population. "Number of subjects analyzed" reflects the total number of participants who provided evaluable data at any timepoint. The number of participants who provided evaluable data for the analysis at each timepoint (n) is shown in the table. Values entered as "99999" mean that the calculation was not performed because no participants provided data for the visit.

End point type	Secondary

End point timeframe:

Baseline; Weeks 1, 2, 4, 8, 12, 18, 24, 30, 36, 42, 48; FU Weeks 4, 12, 24 (up to 72 weeks overall)

Notes:

[48] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	49		
Units: standard deviations				
arithmetic mean (standard deviation)				
Baseline (n=101,49)	0.106 (± 1.154)	-0.047 (± 1.154)		
Week 1 (n=100,0	-0.024 (± 0.089)	99999 (± 99999)		
Week 2 (n=99,0)	-0.023 (± 0.108)	99999 (± 99999)		
Week 4 (n=101,0)	-0.048 (± 0.158)	99999 (± 99999)		
Week 8 (n=101,0)	-0.082 (± 0.228)	99999 (± 99999)		
Week 12 (n=99,48)	-0.09 (± 0.267)	-0.04 (± 0.241)		
Week 18 (n=99,0)	-0.155 (± 0.309)	99999 (± 99999)		
Week 24 (n=100,47)	-0.165 (± 0.35)	-0.09 (± 0.323)		
Week 30 (n=99,0)	-0.189 (± 0.372)	99999 (± 99999)		
Week 36 (n=97,48)	-0.192 (± 0.395)	-0.057 (± 0.338)		
Week 42 (n=99,0)	-0.24 (± 0.375)	99999 (± 99999)		
Week 48 (n=96,47)	-0.214 (± 0.371)	-0.082 (± 0.343)		
FU Week 4 (n=99,0)	-0.156 (± 0.346)	99999 (± 99999)		
FU Week 12 (n=101,24)	-0.089 (± 0.384)	-0.263 (± 0.333)		
FU Week 24 (n=100,15)	-0.046 (± 0.452)	-0.322 (± 0.325)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Height for Age Z-Score in Group C

End point title	Change From Baseline in Height for Age Z-Score in Group C[49]

End point description:

The difference between the population mean and raw scores was calculated as the height for age z-score. Mean absolute values at Baseline were reported. The change from Baseline to each visit was averaged among all participants and expressed in units of standard deviations. Safety Population.

End point type	Secondary

End point timeframe:

Baseline; Weeks 12, 24, 36, 48; FU Weeks 12, 24 (up to 72 weeks overall)

Notes:

[49] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: standard deviations				
arithmetic mean (standard deviation)				
Baseline	0.586 (± 0.947)			
Week 12	0.07 (± 0.492)			
Week 24	0.262 (± 0.42)			
Week 36	0.3 (± 0.601)			
Week 48	0.19 (± 0.683)			
FU Week 12	0.205 (± 0.611)			
FU Week 24	0.064 (± 0.634)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Weight for Age Z-Score in Group C

End point title	Change From Baseline in Weight for Age Z-Score in Group C[50]

End point description:

The difference between the population mean and raw scores was calculated as the weight for age z-score. Mean absolute values at Baseline were reported. The change from Baseline to each visit was averaged among all participants and expressed in units of standard deviations. Safety Population. The number of participants who provided evaluable data for the analysis at each timepoint (n) is shown in the table.

End point type	Secondary

End point timeframe:

Baseline; Weeks 1, 2, 4, 8, 12, 18, 24, 30, 36, 42, 48; FU Weeks 4, 12, 24 (up to 72 weeks overall)

Notes:

[50] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried

out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: standard deviations				
arithmetic mean (standard deviation)				
Baseline (n=10)	0.187 (± 1.141)			
Week 1 (n=9)	-0.044 (± 0.052)			
Week 2 (n=10)	-0.023 (± 0.107)			
Week 4 (n=10)	0.049 (± 0.243)			
Week 8 (n=10)	-0.041 (± 0.198)			
Week 12 (n=10)	0.012 (± 0.288)			
Week 18 (n=10)	-0.018 (± 0.377)			
Week 24 (n=10)	-0.089 (± 0.245)			
Week 30 (n=10)	-0.094 (± 0.34)			
Week 36 (n=10)	0 (± 0.443)			
Week 42 (n=10)	-0.032 (± 0.344)			
Week 48 (n=10)	-0.208 (± 0.374)			
FU Week 4 (n=10)	-0.054 (± 0.35)			
FU Week 12 (n=10)	-0.156 (± 0.29)			
FU Week 24 (n=10)	-0.161 (± 0.309)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HBeAg Seroconversion at 24 Weeks After EOT in Group C

End point title	Percentage of Participants With HBeAg Seroconversion at 24 Weeks After EOT in Group C[51]

End point description:

HBeAg seroconversion was defined as loss of HBeAg and the presence of anti-HBe. The percentage of participants with HBeAg seroconversion at 24 weeks after EOT was reported. The 95% CI was calculated by the Pearson-Clopper method. Safety Population.

End point type	Secondary

End point timeframe:

FU Week 24 (up to 72 weeks overall)

Notes:

[51] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of participants				
number (confidence interval 95%)	30 (6.67 to 65.25)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Quantitative Serum ALT Level in Groups A and B

End point title	Change From Baseline in Quantitative Serum ALT Level in Groups A and B[52]

End point description:

The change in quantitative ALT from Baseline to each visit was averaged among all participants and expressed as a factor of the laboratory-specific ULN (for example, 1 × ULN, 2 × ULN, 3 × ULN). ITT Population. All participants were included in the endpoint analysis. The number of participants who provided evaluable data for the analysis at each timepoint (n) is shown in the table. Values entered as "99999" mean that the calculation was not performed because no participants provided data for the visit.

End point type	Secondary

End point timeframe:

Weeks 1, 2, 4, 8, 12, 18, 24, 30, 36, 42, 48; FU Weeks 4, 12, 24 (up to 72 weeks overall)

Notes:

[52] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	50		
Units: factor of ULN				
arithmetic mean (standard deviation)				

Week 1 (n=98,0)	0.606 (± 1.565)	99999 (± 99999)		
Week 2 (n=99,0)	0.06 (± 2.283)	99999 (± 99999)		
Week 4 (n=101,0)	0.564 (± 3.026)	99999 (± 99999)		
Week 8 (n=100,0)	0.463 (± 3.225)	99999 (± 99999)		
Week 12 (n=97,49)	0.415 (± 3.732)	0.598 (± 5.934)		
Week 18 (n=98,0)	0.288 (± 3.332)	99999 (± 99999)		
Week 24 (n=99,47)	0.004 (± 3.496)	-0.462 (± 2.311)		
Week 30 (n=98,0)	-0.1 (± 3.163)	99999 (± 99999)		
Week 36 (n=99,47)	-0.302 (± 2.8)	-0.51 (± 1.835)		
Week 42 (n=99,0)	-0.436 (± 2.732)	99999 (± 99999)		
Week 48 (n=99,46)	-0.63 (± 2.652)	-0.939 (± 1.914)		
FU Week 4 (n=99,0)	-1.474 (± 2.889)	99999 (± 99999)		
FU Week 12 (n=100,0)	-0.736 (± 2.972)	99999 (± 99999)		
FU Week 24 (n=101,15)	-1.302 (± 2.766)	-0.701 (± 2.22)		

Statistical analyses

No statistical analyses for this end point

Secondary: Quantitative HBeAg Level in Groups A and B

End point title	Quantitative HBeAg Level in Groups A and B[53]

End point description:

Quantitative HBeAg at each visit was averaged among all participants and expressed in log10 Paul Ehrlich Institute units per milliliter (PEIU/mL). ITT Population. All participants were included in the endpoint analysis. The number of participants who provided evaluable data for the analysis at each timepoint (n) is shown in the table.

End point type	Secondary

End point timeframe:

Baseline; Weeks 12, 24, 36, 48; FU Week 24 (up to 72 weeks overall)

Notes:

[53] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	50		
Units: log10 PEIU/mL				
arithmetic mean (standard deviation)				
Baseline (n=92,43)	2.736 (± 0.502)	2.568 (± 0.65)		
Week 12 (n=90,45)	2.09 (± 0.879)	2.391 (± 0.878)		
Week 24 (n=93,41)	1.865 (± 0.956)	2.36 (± 0.896)		
Week 36 (n=90,41)	1.604 (± 0.991)	2.272 (± 0.985)		
Week 48 (n=98,46)	1.466 (± 1.053)	2.124 (± 1.091)		
FU Week 24 (n=100,14)	1.537 (± 1.334)	2.217 (± 1.395)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Quantitative HBeAg Level in Groups A and B

End point title	Change From Baseline in Quantitative HBeAg Level in Groups A and B[54]

End point description:

The change in quantitative HBeAg from Baseline to each visit was averaged among all participants and expressed in log10 PEIU/mL. ITT Population. "Number of subjects analyzed" reflects the total number of participants who provided evaluable data at any timepoint. The number of participants who provided evaluable data for the analysis at each timepoint (n) is shown in the table.

End point type	Secondary

End point timeframe:

Weeks 12, 24, 36, 48; FU Week 24 (up to 72 weeks overall)

Notes:

[54] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	92	43		
Units: log10 PEIU/mL				
arithmetic mean (standard deviation)				

Week 12 (n=84,39)	-0.583 (± 0.672)	-0.225 (± 0.497)		
Week 24 (n=84,36)	-0.834 (± 0.805)	-0.261 (± 0.612)		
Week 36 (n=81,37)	1.123 (± 0.91)	-0.3 (± 0.621)		
Week 48 (n=89,42)	-1.28 (± 1.043)	-0.491 (± 0.74)		
FU Week 24 (n=91,13)	-1.24 (± 1.205)	-0.452 (± 0.793)		

Statistical analyses

No statistical analyses for this end point

Secondary: Quantitative HBsAg Level in Groups A and B

End point title	Quantitative HBsAg Level in Groups A and B[55]

End point description:

Quantitative HBsAg at each visit was averaged among all participants and expressed in log10 IU/mL. ITT Population. All participants were included in the endpoint analysis. The number of participants who provided evaluable data for the analysis at each timepoint (n) is shown in the table.

End point type	Secondary

End point timeframe:

Baseline; Weeks 12, 24, 36, 48; FU Week 24 (up to 72 weeks overall)

Notes:

[55] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	50		
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Baseline (n=101,44)	4.309 (± 0.687)	4.383 (± 0.721)		
Week 12 (n=97,49)	3.844 (± 1.186)	4.299 (± 0.809)		
Week 24 (n=99,46)	3.509 (± 1.507)	4.336 (± 0.732)		
Week 36 (n=99,47)	3.265 (± 1.661)	4.272 (± 0.726)		
Week 48 (n=99,47	3.078 (± 1.769)	4.215 (± 0.718)		
FU Week 24 (n=100,14)	3.37 (± 1.63)	4.394 (± 0.939)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Quantitative HBsAg Level in Groups A and B

End point title	Change From Baseline in Quantitative HBsAg Level in Groups A and B[56]

End point description:

The change in quantitative HBsAg from Baseline to each visit was averaged among all participants and expressed in log10 IU/mL. ITT Population. "Number of subjects analyzed" reflects the total number of participants who provided evaluable data at any timepoint. The number of participants who provided evaluable data for the analysis at each timepoint (n) is shown in the table.

End point type	Secondary

End point timeframe:

Weeks 12, 24, 36, 48; FU Week 24 (up to 72 weeks overall)

Notes:

[56] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	44		
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Week 12 (n=97,44)	-0.444 (± 1.021)	-0.081 (± 0.356)		
Week 24 (n=99,42)	-0.798 (± 1.343)	-0.032 (± 0.392)		
Week 36 (n=99,44)	-1.051 (± 1.534)	-0.126 (± 0.26)		
Week 48 (n=99,44)	-1.239 (± 1.652)	-0.188 (± 0.285)		
FU Week 24 (n=100,13)	-0.936 (± 1.491)	-0.204 (± 0.316)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Quantitative Serum ALT Level in Group C

End point title	Change From Baseline in Quantitative Serum ALT Level in Group C[57]

End point description:

The change in quantitative ALT from Baseline to each visit was averaged among all participants and expressed as a factor of the laboratory-specific ULN (for example, 1 × ULN, 2 × ULN, 3 × ULN). Safety Population. The number of participants who provided evaluable data for the analysis at each timepoint (n) is shown in the table.

End point type	Secondary

End point timeframe:

Weeks 1, 2, 4, 8, 12, 18, 24, 30, 36, 42, 48; FU Weeks 4, 12, 24 (up to 72 weeks overall)

Notes:

[57] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: factor of ULN				
arithmetic mean (standard deviation)				
Week 1 (n=10)	0.313 (± 0.414)			
Week 2 (n=10)	0.091 (± 0.991)			
Week 4 (n=10)	-0.361 (± 1.566)			
Week 8 (n=10)	-0.101 (± 1.895)			
Week 12 (n=10)	-0.012 (± 1.613)			
Week 18 (n=10)	-0.589 (± 0.996)			
Week 24 (n=10)	-0.917 (± 1.31)			
Week 30 (n=10)	-0.584 (± 1.73)			
Week 36 (n=10)	-0.633 (± 1.455)			
Week 42 (n=10)	-1.211 (± 1.05)			
Week 48 (n=9)	-1.104 (± 1.084)			
FU Week 4 (n=10)	-1.669 (± 0.95)			
FU Week 12 (n=10)	-1.283 (± 1.501)			
FU Week 24 (n=10)	-1.256 (± 1.757)			

Statistical analyses

No statistical analyses for this end point

Secondary: Quantitative HBeAg Level in Group C

End point title	Quantitative HBeAg Level in Group C[58]

End point description:

Quantitative HBeAg at each visit was averaged among all participants and expressed in log10 PEIU/mL. Safety Population. The number of participants who provided evaluable data for the analysis at each timepoint (n) is shown in the table.

End point type	Secondary

End point timeframe:

Baseline; Weeks 12, 24, 36, 48; FU Week 24 (up to 72 weeks overall)

Notes:

[58] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: log10 PEIU/mL				
arithmetic mean (standard deviation)				
Baseline (n=9)	2.344 (± 0.981)			
Week 12 (n=9)	1.62 (± 1.288)			
Week 24 (n=9)	1.802 (± 1.14)			
Week 36 (n=10)	1.561 (± 1.178)			
Week 48 (n=10)	1.429 (± 1.259)			
FU Week 24 (n=10)	1.442 (± 1.416)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Quantitative HBeAg Level in Group C

End point title	Change From Baseline in Quantitative HBeAg Level in Group

End point description:

The change in quantitative HBeAg from Baseline to each visit was averaged among all participants and expressed in log10 PEIU/mL. Safety Population. "Number of subjects analyzed" reflects the total number of participants who provided evaluable data at any timepoint. The number of participants who provided evaluable data for the analysis at each timepoint (n) is shown in the table.

End point type	Secondary

End point timeframe:

Weeks 12, 24, 36, 48; FU Week 24 (up to 72 weeks overall)

Notes:

[59] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: log10 PEIU/mL				
arithmetic mean (standard deviation)				
Week 12 (n=8)	-0.779 (± 0.645)			
Week 24 (n=8)	-0.817 (± 0.678)			
Week 36 (n=9)	-0.817 (± 0.685)			
Week 48 (n=9)	-0.762 (± 0.818)			
FU Week 24 (n=9)	-0.742 (± 0.84)			

Statistical analyses

No statistical analyses for this end point

Secondary: Quantitative HBsAg Level in Group C

End point title	Quantitative HBsAg Level in Group C[60]

End point description:

Quantitative HBsAg at each visit was averaged among all participants and expressed in log10 IU/mL. Safety Population.

End point type	Secondary

End point timeframe:

Baseline; Weeks 12, 24, 36, 48; FU Week 24 (up to 72 weeks overall)

Notes:

[60] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Baseline	4.225 (± 0.518)			
Week 12	3.829 (± 0.589)			
Week 24	3.515 (± 1.113)			
Week 36	3.282 (± 1.263)			
Week 48	3.215 (± 1.352)			
FU Week 24	3.137 (± 1.463)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Quantitative HBsAg Level in Group C

End point title	Change From Baseline in Quantitative HBsAg Level in Group

End point description:

The change in quantitative HBsAg from Baseline to each visit was averaged among all participants and expressed in log10 IU/mL. Safety Population.

End point type	Secondary

End point timeframe:

Weeks 12, 24, 36, 48; FU Week 24 (up to 72 weeks overall)

Notes:

[61] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group C: PEG-IFN Monotherapy With Advanced Fibrosis			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Week 12	-0.397 (± 0.428)			
Week 24	-0.71 (± 0.712)			

Week 36	-0.943 (± 0.913)			
Week 48	-1.01 (± 1.019)			
FU Week 24	-1.088 (± 1.141)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HBeAg Seroconversion Over Time in Groups A and B

End point title	Percentage of Participants with HBeAg Seroconversion Over Time in Groups A and B[62]

End point description:

HBeAg seroconversion was defined as loss of HBeAg and the presence of anti-HBe. The 95% CI was calculated by the Pearson-Clopper method. ITT Population.

End point type	Secondary

End point timeframe:

Baseline, FU Years: 1, 2, 3, 4, 5

Notes:

[62] - 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: Justification: Groups A an B were randomized and formal statistical analyses were carried out to compare the arms. Participants in Group C were allocated to treatment for ethical reasons, and only descriptive results were reported.

End point values	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	50		
Units: percentage of subjects				
number (confidence interval 95%)				
Baseline	0.00 (0.00 to 3.59)	0.00 (0.00 to 7.11)		
Fu Year 1	32.7 (23.67 to 42.72)	6.08 (1.25 to 16.55)		
Fu Year 2	33.7 (24.56 to 43.75)	6.08 (1.25 to 16.55)		
Fu Year 3	46.5 (36.55 to 56.73)	6.08 (1.25 to 16.55)		
Fu Year 4	30.7 (21.90 to 40.66)	8.00 (2.22 to 19.23)		
Fu Year 5	5.9 (2.21 to 12.48)	0.00 (0.00 to 7.11)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Loss of HBeAg at 24 Weeks after the End of Switch Treatment Period: Switch Group

End point title	Percentage of Participants with Loss of HBeAg at 24 Weeks after the End of Switch Treatment Period: Switch Group

End point description:

The percentage of participants with loss of HBeAg at 24 weeks after EOT/POP was reported. The 95% CI was calculated by the Pearson-Clopper method. ITT Population.

End point type	Secondary

End point timeframe:

FU Week 24 (up to 72 weeks overall)

End point values	Group D: Switch to PEG-IFN Monotherapy			
Subject group type	Subject analysis set			
Number of subjects analysed	33			
Units: percentage of participants				
number (confidence interval 95%)	30.3 (15.59 to 48.71)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HBsAg Seroconversion at 24 Weeks after the End of Switch Treatment Period: Switch Group

End point title	Percentage of Participants with HBsAg Seroconversion at 24 Weeks after the End of Switch Treatment Period: Switch Group

End point description:

HBeAg seroconversion was defined as loss of HBeAg and the presence of hepatitis B envelope antibody (anti-HBe). The percentage of participants with HBeAg seroconversion at 24 weeks after EOT/POP was reported. The 95 percent (%) confidence interval (CI) was calculated by the Pearson-Clopper method. Intent-to-Treat (ITT) Population: All randomized participants regardless of treatment received.

End point type	Secondary

End point timeframe:

FU Week 24 (up to 72 weeks overall)

End point values	Group D: Switch to PEG-IFN Monotherapy			
Subject group type	Subject analysis set			
Number of subjects analysed	33			
Units: percentage of participants				

number (confidence interval 95%)	9.1 (1.92 to 24.33)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Loss of HBsAg at 24 Weeks after the End of Switch Treatment Period: Switch Group

End point title	Percentage of Participants with Loss of HBsAg at 24 Weeks after the End of Switch Treatment Period: Switch Group

End point description:

HBeAg seroconversion was defined as loss of HBeAg and the presence of hepatitis B envelope antibody (anti-HBe). The percentage of participants with HBeAg seroconversion at 24 weeks after EOT/POP was reported. The 95 percent (%) confidence interval (CI) was calculated by the Pearson-Clopper method. Intent-to-Treat (ITT) Population: All randomized participants regardless of treatment received.

End point type	Secondary

End point timeframe:

FU Week 24 (up to 72 weeks overall)

End point values	Group D: Switch to PEG-IFN Monotherapy			
Subject group type	Subject analysis set			
Number of subjects analysed	33			
Units: percentage of participants				
number (confidence interval 95%)	12.1 (3.40 to 28.20)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HBV Deoxyribonucleic Acid (DNA) <20,000 International Units per Milliliter (IU/mL) at 24 Weeks after the End of Switch Treatment Period: Switch Group

End point title	Percentage of Participants with HBV Deoxyribonucleic Acid (DNA) <20,000 International Units per Milliliter (IU/mL) at 24 Weeks after the End of Switch Treatment Period: Switch Group

End point description:

HBV DNA was quantified using polymerase chain reaction (PCR) by Roche Taqman. The percentage of participants with HBV DNA <20,000 IU/mL at 24 weeks after EOT/POP was reported. The 95% CI was calculated by the Pearson-Clopper method. ITT Population.

End point type	Secondary

End point timeframe:

FU Week 24 (up to 72 weeks overall)

End point values	Group D: Switch to PEG-IFN Monotherapy			
Subject group type	Subject analysis set			
Number of subjects analysed	33			
Units: percentage of participants				
number (confidence interval 95%)	36.4 (20.40 to 54.88)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Normal ALT at 24 Weeks after the End of Switch Treatment Period: Switch Group

End point title	Percentage of Participants with Normal ALT at 24 Weeks after the End of Switch Treatment Period: Switch Group

End point description:

Normal ALT was defined as ALT ≤ ULN, where each ULN was given by the laboratory at which the sample was analyzed. The percentage of participants with normal ALT at EOT/POP was reported. The 95% CI was calculated by the Pearson-Clopper method. ITT Population.

End point type	Secondary

End point timeframe:

FU Week 24 (up to 72 weeks overall)

End point values	Group D: Switch to PEG-IFN Monotherapy			
Subject group type	Subject analysis set			
Number of subjects analysed	33			
Units: percentage of participants				
number (confidence interval 95%)	30.3 (15.59 to 48.71)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HBV DNA <2,000 IU/mL at 24 Weeks after the End of Switch Treatment Period: Switch Group

End point title	Percentage of Participants with HBV DNA <2,000 IU/mL at 24 Weeks after the End of Switch Treatment Period: Switch Group

End point description:

HBV DNA was quantified using PCR by Roche Taqman. The percentage of participants with HBV DNA <2,000 IU/mL at 24 weeks after EOT/POP was reported. The 95% CI was calculated by the Pearson-Clopper method. ITT Population.

End point type	Secondary

End point timeframe:

FU Week 24 (up to 72 weeks overall)

End point values	Group D: Switch to PEG-IFN Monotherapy			
Subject group type	Subject analysis set			
Number of subjects analysed	33			
Units: percentage of participants				
number (confidence interval 95%)	27.3 (13.30 to 45.52)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HBV DNA Undetectable at 24 Weeks after the End of Switch Treatment Period: Switch Group

End point title	Percentage of Participants with HBV DNA Undetectable at 24 Weeks after the End of Switch Treatment Period: Switch Group

End point description:

HBV DNA was quantified using PCR by Roche Taqman. Undetectable HBV DNA was defined as HBV DNA <29 IU/mL. The percentage of participants with HBV DNA undetectable at 24 weeks after EOT/POP was reported. The 95% CI was calculated by the Pearson-Clopper method. ITT Population.

End point type	Secondary

End point timeframe:

FU Week 24 (up to 72 weeks overall)

End point values	Group D: Switch to PEG-IFN Monotherapy			
Subject group type	Subject analysis set			
Number of subjects analysed	33			
Units: percentage of participants				
number (confidence interval 95%)	18.2 (6.98 to 35.46)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Combined HBeAg Seroconversion and HBV DNA <20,000 IU/mL at 24 Weeks after the End of Switch Treatment Period: Switch Group

End point title	Percentage of Participants with Combined HBeAg Seroconversion and HBV DNA <20,000 IU/mL at 24 Weeks after the End of Switch Treatment Period: Switch Group

End point description:

HBeAg seroconversion was defined as loss of HBeAg and the presence of anti-HBe. HBV DNA was quantified using PCR by Roche Taqman. The 95% CI was calculated by the Pearson-Clopper method. ITT Population.

End point type	Secondary

End point timeframe:

FU Week 24 (up to 72 weeks overall)

End point values	Group D: Switch to PEG-IFN Monotherapy			
Subject group type	Subject analysis set			
Number of subjects analysed	33			
Units: percentage of participants				
number (confidence interval 95%)	27.3 (13.30 to 45.52)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Combined HBeAg Seroconversion and HBV DNA <2,000 IU/mL at 24 Weeks after the End of Switch Treatment Period: Switch Group

End point title	Percentage of Participants with Combined HBeAg Seroconversion and HBV DNA <2,000 IU/mL at 24 Weeks after the End of Switch Treatment Period: Switch Group

End point description:

HBeAg seroconversion was defined as loss of HBeAg and the presence of anti-HBe. HBV DNA was quantified using PCR by Roche Taqman. The percentage of participants with combined HBeAg seroconversion and HBV DNA <2,000 IU/mL at 24 weeks after EOT/POP was reported. The 95% CI was calculated by the Pearson-Clopper method. ITT Population.

End point type	Secondary

End point timeframe:

FU Week 24 (up to 72 weeks overall)

End point values	Group D: Switch to PEG-IFN Monotherapy			
Subject group type	Subject analysis set			
Number of subjects analysed	33			
Units: percentage of participants				
number (confidence interval 95%)	21.2 (8.98 to 38.91)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline to FU Week 24 (up to 72 weeks overall)

Adverse event reporting additional description:

Safety Population

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis

Reporting group description:

Participants without advanced fibrosis were randomized and received PEG-IFN monotherapy for 48 weeks with a 24-week follow-up and an additional ongoing 4.5-year extended follow-up. Each dose of 45 to 180 mcg was based on BSA and given as a once-weekly SC injection for 48 weeks. BSA-based dosing was as follows: 0.51-0.53 m^2, 45 mcg; 0.54-0.74 m^2, 65 mcg; 0.75-1.08 m^2, 90 mcg; 1.09-1.51 m^2, 135 mcg; >1.51 m^2, 180 mcg.

Reporting group title	Group B: Untreated Control Without Advanced Fibrosis

Reporting group description:

Participants without advanced fibrosis were randomized and were evaluated for 48 weeks with a 24-week follow-up and an additional ongoing 4.5-year extended follow-up. As the study is open-label, participants did not receive any investigational or placebo treatment during the 48-week POP. For ethical reasons, participants in Group B had a reduced visit schedule (every 12 weeks) compared to participants in Group A through the end of 24-week follow-up.

Reporting group title	Group C: PEG-IFN Monotherapy With Advanced Fibrosis

Reporting group description:

Participants with advanced fibrosis were allocated (not randomized) to receive PEG-IFN monotherapy for 48 weeks with a 24-week follow-up and an additional ongoing 4.5-year extended follow-up. Each dose of 45 to 180 mcg was based on BSA and given as a once-weekly SC injection for 48 weeks. BSA-based dosing was as follows: 0.51-0.53 m^2, 45 mcg; 0.54-0.74 m^2, 65 mcg; 0.75-1.08 m^2, 90 mcg; 1.09-1.51 m^2, 135 mcg; >1.51 m^2, 180 mcg.

Reporting group title	Group D: Switch to PEG-IFN Monotherapy

Reporting group description:

Participants without advanced fibrosis who did not receive treatment and had not experienced HBeAg seroconversion were allowed to switch to PEG-IFN monotherapy. Treatment was given over 48 weeks with a 24-week follow-up and an additional ongoing 4.5-year extended follow-up. Each dose of 45 to 180 mcg was based on BSA and given as a once-weekly SC injection for 48 weeks. BSA-based dosing was as follows: 0.51-0.53 m^2, 45 mcg; 0.54-0.74 m^2, 65 mcg; 0.75-1.08 m^2, 90 mcg; 1.09-1.51 m^2, 135 mcg; >1.51 m^2, 180 mcg.

Reporting group title	Group A - Long Term Follow-up

Reporting group description:

Participants without advanced fibrosis: 4.5-year extended follow-up

Reporting group title	Group B - Long Term Follow-up

Reporting group description:

Participants without advanced fibrosis: 4.5-year extended follow-up

Reporting group title	Group C Long Term Follow-up

Reporting group description:

Participants with advanced fibrosis: 4.5-year extended follow-up

Reporting group title	Group D - Long Term Follow-up

Reporting group description:

Participants without advanced fibrosis who did not receive treatment and had not experienced HBeAg seroconversion were allowed to switch to PEG-IFN monotherapy: 4.5-year extended follow-up

Serious adverse events	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis	Group C: PEG-IFN Monotherapy With Advanced Fibrosis
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 101 (5.94%)	1 / 49 (2.04%)	0 / 10 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 101 (0.99%)	0 / 49 (0.00%)	0 / 10 (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
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 101 (0.99%)	0 / 49 (0.00%)	0 / 10 (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
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	0 / 101 (0.00%)	1 / 49 (2.04%)	0 / 10 (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
Renal and urinary disorders			
Nephropathy			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteochondrosis			
subjects affected / exposed	1 / 101 (0.99%)	0 / 49 (0.00%)	0 / 10 (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
Infections and infestations			
Hepatitis B			

subjects affected / exposed	1 / 101 (0.99%)	0 / 49 (0.00%)	0 / 10 (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
Latent tuberculosis			
subjects affected / exposed	1 / 101 (0.99%)	0 / 49 (0.00%)	0 / 10 (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
Microsporum infection			
subjects affected / exposed	1 / 101 (0.99%)	0 / 49 (0.00%)	0 / 10 (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
Pneumonia			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	1 / 101 (0.99%)	0 / 49 (0.00%)	0 / 10 (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

Serious adverse events	Group D: Switch to PEG-IFN Monotherapy	Group A - Long Term Follow-up	Group B - Long Term Follow-up
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 33 (6.06%)	0 / 101 (0.00%)	0 / 49 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			

subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephropathy			
subjects affected / exposed	1 / 33 (3.03%)	0 / 101 (0.00%)	0 / 49 (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			
Osteochondrosis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Hepatitis B			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Latent tuberculosis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Microsporum infection			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	1 / 33 (3.03%)	0 / 101 (0.00%)	0 / 49 (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
Tonsillitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Group C Long Term Follow-up	Group D - Long Term Follow-up	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	2 / 33 (6.06%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (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			
Nephropathy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (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			
Osteochondrosis			

subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (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			
Hepatitis B			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Latent tuberculosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microsporum infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (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	Group A: PEG-IFN Monotherapy Without Advanced Fibrosis	Group B: Untreated Control Without Advanced Fibrosis	Group C: PEG-IFN Monotherapy With Advanced Fibrosis
Total subjects affected by non-serious adverse events			
subjects affected / exposed	80 / 101 (79.21%)	18 / 49 (36.73%)	9 / 10 (90.00%)
Vascular disorders			
Hypertension			

subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Haematoma			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	10 / 101 (9.90%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	26	0	0
Fatigue			
subjects affected / exposed	9 / 101 (8.91%)	2 / 49 (4.08%)	0 / 10 (0.00%)
occurrences (all)	12	2	0
Influenza like illness			
subjects affected / exposed	15 / 101 (14.85%)	1 / 49 (2.04%)	0 / 10 (0.00%)
occurrences (all)	18	1	0
Injection site pain			
subjects affected / exposed	3 / 101 (2.97%)	0 / 49 (0.00%)	1 / 10 (10.00%)
occurrences (all)	3	0	1
Pyrexia			
subjects affected / exposed	49 / 101 (48.51%)	5 / 49 (10.20%)	8 / 10 (80.00%)
occurrences (all)	107	8	14
Peripheral swelling			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Injection site induration			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Injection site pruritus			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			

Seasonal allergy			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	14 / 101 (13.86%)	3 / 49 (6.12%)	3 / 10 (30.00%)
occurrences (all)	17	3	3
Oropharyngeal pain			
subjects affected / exposed	3 / 101 (2.97%)	3 / 49 (6.12%)	1 / 10 (10.00%)
occurrences (all)	3	4	1
Rhinorrhoea			
subjects affected / exposed	6 / 101 (5.94%)	4 / 49 (8.16%)	0 / 10 (0.00%)
occurrences (all)	6	6	0
Epistaxis			
subjects affected / exposed	8 / 101 (7.92%)	0 / 49 (0.00%)	2 / 10 (20.00%)
occurrences (all)	8	0	2
Asthma			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Irritability			
subjects affected / exposed	1 / 101 (0.99%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Mood altered			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	9 / 101 (8.91%)	4 / 49 (8.16%)	1 / 10 (10.00%)
occurrences (all)	10	4	1
Aspartate aminotransferase increased			
subjects affected / exposed	9 / 101 (8.91%)	3 / 49 (6.12%)	1 / 10 (10.00%)
occurrences (all)	10	3	1

Body temperature increased			
subjects affected / exposed	2 / 101 (1.98%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	4	0	0
Alpha hydroxybutyrate dehydrogenase increased			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase mb increased			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hepatitis B DNA increased			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	5 / 101 (4.95%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	8	0	0
Joint injury			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Expired product administered			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			

Duane's syndrome			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	6 / 101 (5.94%)	1 / 49 (2.04%)	1 / 10 (10.00%)
occurrences (all)	20	1	1
Headache			
subjects affected / exposed	30 / 101 (29.70%)	2 / 49 (4.08%)	4 / 10 (40.00%)
occurrences (all)	71	2	9
Disturbance in attention			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Seizure			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	2 / 101 (1.98%)	0 / 49 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	2
Thrombocytopenia			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Hypermetropia			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Accommodation disorder			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Amblyopia			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Astigmatism			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Erythema of eyelid			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Periorbital swelling			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	19 / 101 (18.81%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	30	0	0
Nausea			
subjects affected / exposed	7 / 101 (6.93%)	0 / 49 (0.00%)	3 / 10 (30.00%)
occurrences (all)	10	0	6
Vomiting			
subjects affected / exposed	14 / 101 (13.86%)	0 / 49 (0.00%)	3 / 10 (30.00%)
occurrences (all)	16	0	4
Abdominal discomfort			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Food poisoning			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Aphthous ulcer			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			

Alopecia			
subjects affected / exposed	6 / 101 (5.94%)	0 / 49 (0.00%)	1 / 10 (10.00%)
occurrences (all)	9	0	1
Pruritus			
subjects affected / exposed	3 / 101 (2.97%)	0 / 49 (0.00%)	1 / 10 (10.00%)
occurrences (all)	4	0	1
Rash			
subjects affected / exposed	10 / 101 (9.90%)	0 / 49 (0.00%)	1 / 10 (10.00%)
occurrences (all)	14	0	2
Eczema			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lichen planus			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin depigmentation			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Urticardia			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Xeroderma			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Renal cyst			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 101 (2.97%)	0 / 49 (0.00%)	1 / 10 (10.00%)
occurrences (all)	5	0	1
Pain in extremity			

subjects affected / exposed	2 / 101 (1.98%)	1 / 49 (2.04%)	1 / 10 (10.00%)
occurrences (all)	2	1	2
Back pain			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Scoliosis			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	7 / 101 (6.93%)	1 / 49 (2.04%)	0 / 10 (0.00%)
occurrences (all)	17	1	0
Oral herpes			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	9 / 101 (8.91%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	14	0	0
Viral infection			
subjects affected / exposed	0 / 101 (0.00%)	1 / 49 (2.04%)	1 / 10 (10.00%)
occurrences (all)	0	2	1
Peritonsillar abscess			
subjects affected / exposed	1 / 101 (0.99%)	0 / 49 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Chronic sinusitis			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gingiviti			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Helminthic infection			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection viral			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tuberculous pleurisy			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 101 (0.00%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	7 / 101 (6.93%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	7	0	0

Non-serious adverse events	Group D: Switch to PEG-IFN Monotherapy	Group A - Long Term Follow-up	Group B - Long Term Follow-up
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 33 (63.64%)	25 / 101 (24.75%)	6 / 49 (12.24%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0

General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 33 (12.12%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	8	0	0
Fatigue			
subjects affected / exposed	3 / 33 (9.09%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	3	0	0
Influenza like illness			
subjects affected / exposed	1 / 33 (3.03%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	1	1	0
Injection site pain			
subjects affected / exposed	1 / 33 (3.03%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	17 / 33 (51.52%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	35	1	0
Peripheral swelling			
subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Injection site induration			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Injection site pruritus			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 33 (3.03%)	2 / 101 (1.98%)	0 / 49 (0.00%)
occurrences (all)	1	2	0

Oropharyngeal pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	2 / 33 (6.06%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	2	0	0
Epistaxis			
subjects affected / exposed	2 / 33 (6.06%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	2	0	0
Asthma			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	2 / 49 (4.08%)
occurrences (all)	0	0	2
Psychiatric disorders			
Irritability			
subjects affected / exposed	2 / 33 (6.06%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	2	0	0
Insomnia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Mood altered			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 33 (6.06%)	3 / 101 (2.97%)	0 / 49 (0.00%)
occurrences (all)	2	3	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 33 (3.03%)	2 / 101 (1.98%)	0 / 49 (0.00%)
occurrences (all)	1	2	0
Body temperature increased			
subjects affected / exposed	3 / 33 (9.09%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	3	0	0
Alpha hydroxybutyrate dehydrogenase increased			
subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Blood creatine phosphokinase			

increased			
subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Blood creatine phosphokinase mb increased			
subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Hepatitis B DNA increased			
subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 33 (6.06%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	2	0	0
Joint injury			
subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Expired product administered			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Duane's syndrome			
subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Tachycardia			

subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 33 (3.03%)	0 / 101 (0.00%)	1 / 49 (2.04%)
occurrences (all)	1	0	1
Headache			
subjects affected / exposed	11 / 33 (33.33%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	14	1	0
Disturbance in attention			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Seizure			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	2 / 33 (6.06%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	2	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Hypermetropia			
subjects affected / exposed	0 / 33 (0.00%)	2 / 101 (1.98%)	0 / 49 (0.00%)
occurrences (all)	0	2	0
Accommodation disorder			
subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Amblyopia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Astigmatism			
subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Erythema of eyelid			

subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Periorbital swelling			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 33 (12.12%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	6	0	0
Nausea			
subjects affected / exposed	1 / 33 (3.03%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	2 / 33 (6.06%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	2	0	0
Abdominal discomfort			
subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Food poisoning			
subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Aphthous ulcer			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 33 (6.06%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	2	1	0
Pruritus			
subjects affected / exposed	1 / 33 (3.03%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Rash			

subjects affected / exposed	1 / 33 (3.03%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Eczema			
subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Lichen planus			
subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Skin depigmentation			
subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Urticardia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Xeroderma			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	1 / 49 (2.04%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Renal cyst			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	1 / 49 (2.04%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 33 (6.06%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	2	0	0
Pain in extremity			
subjects affected / exposed	2 / 33 (6.06%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	2	0	0
Back pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	1 / 49 (2.04%)
occurrences (all)	0	0	1
Joint swelling			

subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Scoliosis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 33 (9.09%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	4	0	0
Oral herpes			
subjects affected / exposed	3 / 33 (9.09%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	3	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Viral infection			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Peritonsillar abscess			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Chronic sinusitis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Gingiviti			
subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Helminthic infection			
subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection			
subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0

Respiratory tract infection viral			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	1 / 49 (2.04%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Tuberculous pleurisy			
subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Tonsillitis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 101 (0.99%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 33 (3.03%)	0 / 101 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Group C Long Term Follow-up	Group D - Long Term Follow-up	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	27 / 33 (81.82%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Haematoma			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 10 (0.00%)	10 / 33 (30.30%)	
occurrences (all)	0	10	
Fatigue			

subjects affected / exposed	0 / 10 (0.00%)	4 / 33 (12.12%)	
occurrences (all)	0	4	
Influenza like illness			
subjects affected / exposed	0 / 10 (0.00%)	3 / 33 (9.09%)	
occurrences (all)	0	3	
Injection site pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Pyrexia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	41	
Peripheral swelling			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Injection site induration			
subjects affected / exposed	0 / 10 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Injection site pruritus			
subjects affected / exposed	0 / 10 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Rhinorrhoea			

subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Epistaxis			
subjects affected / exposed	0 / 10 (0.00%)	2 / 33 (6.06%)	
occurrences (all)	0	2	
Asthma			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Irritability			
subjects affected / exposed	0 / 10 (0.00%)	3 / 33 (9.09%)	
occurrences (all)	0	3	
Insomnia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Mood altered			
subjects affected / exposed	0 / 10 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 10 (0.00%)	7 / 33 (21.21%)	
occurrences (all)	0	7	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 10 (0.00%)	3 / 33 (9.09%)	
occurrences (all)	0	3	
Body temperature increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Alpha hydroxybutyrate dehydrogenase increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Blood creatine phosphokinase mb			

increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Hepatitis B DNA increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Weight decreased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Joint injury			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Expired product administered			
subjects affected / exposed	0 / 10 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Congenital, familial and genetic disorders			
Duane's syndrome			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 10 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Tachycardia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Nervous system disorders			

Dizziness			
subjects affected / exposed	0 / 10 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	0 / 10 (0.00%)	17 / 33 (51.52%)	
occurrences (all)	0	17	
Disturbance in attention			
subjects affected / exposed	0 / 10 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Seizure			
subjects affected / exposed	0 / 10 (0.00%)	2 / 33 (6.06%)	
occurrences (all)	0	2	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Thrombocytopenia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Eye disorders			
Hypermetropia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Accommodation disorder			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Amblyopia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Astigmatism			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Erythema of eyelid			
subjects affected / exposed	0 / 10 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Eye pain			

subjects affected / exposed	0 / 10 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Periorbital swelling			
subjects affected / exposed	0 / 10 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 10 (0.00%)	2 / 33 (6.06%)	
occurrences (all)	0	2	
Nausea			
subjects affected / exposed	0 / 10 (0.00%)	2 / 33 (6.06%)	
occurrences (all)	0	2	
Vomiting			
subjects affected / exposed	0 / 10 (0.00%)	2 / 33 (6.06%)	
occurrences (all)	0	2	
Abdominal discomfort			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Food poisoning			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Aphthous ulcer			
subjects affected / exposed	0 / 10 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 10 (0.00%)	2 / 33 (6.06%)	
occurrences (all)	0	2	
Pruritus			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Rash			
subjects affected / exposed	0 / 10 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Eczema			

subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Lichen planus			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Skin depigmentation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Urticardia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Xeroderma			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Erythema			
subjects affected / exposed	0 / 10 (0.00%)	3 / 33 (9.09%)	
occurrences (all)	0	3	
Renal and urinary disorders			
Renal cyst			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 10 (0.00%)	2 / 33 (6.06%)	
occurrences (all)	0	2	
Pain in extremity			
subjects affected / exposed	0 / 10 (0.00%)	3 / 33 (9.09%)	
occurrences (all)	0	3	
Back pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Joint swelling			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Scoliosis			

subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Myalgia			
subjects affected / exposed	0 / 10 (0.00%)	6 / 33 (18.18%)	
occurrences (all)	0	6	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 10 (0.00%)	5 / 33 (15.15%)	
occurrences (all)	0	5	
Oral herpes			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Viral infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Peritonsillar abscess			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Chronic sinusitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Gingiviti			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Helminthic infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Respiratory tract infection viral			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	

Rhinitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Tuberculous pleurisy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Tonsillitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Gastroenteritis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 10 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 October 2011	The protocol was amended primarily for the addition of exploratory biomarker objectives. Corresponding laboratory procedures, including the collection of DNA specimens, were added to the study assessments. The timeline for liver elasticity assessment was also expanded to FU Year 2.
04 April 2012	Under this protocol amendment, liver biopsy was now required within 2 years of Baseline to ensure participants had not progressed to cirrhosis, and a liver elasticity assessment was added at EOT/POP. New entry criteria were also added for participants in Group B who opted to switch to PEG-IFN.
17 May 2013	Some liver biopsy assessments were removed to minimize participant discomfort, and ophthalmological examinations could now be performed 6 months before Baseline. Eligibility criteria were also updated for both administrative and safety purposes. Dose reduction guidelines were updated, and additional safety monitoring parameters were added.
28 May 2014	Eligibility criteria were updated including the removal of HBV antibody screening requirements, explanation of normal hemoglobin range, exclusion of participants with renal impairment. Additionally, participants with ALT > 10 × ULN were now excluded from switching to PEG-IFN in Group D. Scoring guidelines for liver fibrosis were also added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported