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	

Results information

Result version number	v1
This version publication date	24 July 2016
First version publication date	24 July 2016

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	Interim
Date of interim/final analysis	09 January 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 January 2016
Global end of trial reached?	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
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	China: 76
Country: Number of subjects enrolled	Israel: 9
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	Germany: 2
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Poland: 4
Country: Number of subjects enrolled	Russian Federation: 19
Country: Number of subjects enrolled	Ukraine: 13

Country: Number of subjects enrolled	United States: 8
Worldwide total number of subjects	161
EEA total number of subjects	26

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?	No
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	No intervention

No investigational medicinal product assigned in this arm

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.

Arm title	All Groups Combined

Arm 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.

Arm type	Experimental or placebo
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	101	26	10
Completed FU Week 24	101	15	10
Completed	0	0	0
Not completed	101	50	10
Ongoing/switched to PEG-IFN	-	33	-
Adverse event	-	1	-
Lost to follow-up	-	1	-
Ongoing in follow-up	101	11	10
Withdrawal by subject	-	4	-

Number of subjects in period 1	All Groups Combined
Started	161
Completed Week 48	156
Completed Follow-Up (FU) Week 12	137

Completed FU Week 24	126
Completed	0
Not completed	161
Ongoing/switched to PEG-IFN	33
Adverse event	1
Lost to follow-up	1
Ongoing in follow-up	122
Withdrawal by subject	4

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 title	All Groups Combined

Reporting group 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.

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			
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	All Groups Combined	Total	

Number of subjects	161	161	
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	10.42		
standard deviation	± 4.73	-	
Gender categorical Units: Subjects			
Female	57	57	
Male	104	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.

Reporting group title	All Groups Combined

Reporting group 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.

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: 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: 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	Fisher's Exact

Statistical analysis description:

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	= 0.0038
Method	Fisher's Exact
Parameter estimate	Odds ratio (OR)
Point estimate	5.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.52
upper limit	29.32

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: 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

Statistical analysis title	Fisher's Exact
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	= 0.0528
Method	Fisher's Exact

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

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

End point description:

The percentage of participants with loss of HBsAg 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: 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)	0 (0 to 7.11)		

Statistical analyses

Statistical analysis title	Fisher's Exact
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	= 0.03
Method	Fisher's Exact

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[5]

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:

[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: 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

Statistical analysis title	Fisher's Exact
Statistical analysis description:	
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	< 0.0001
Method	Fisher's Exact
Parameter estimate	Odds ratio (OR)
Point estimate	7.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.91
upper limit	24.05

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[6]

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:

[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: 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 43.75)	4 (0.49 to 13.71)		

Statistical analyses

Statistical analysis title	Fisher's Exact
Statistical analysis description:	
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	< 0.0001
Method	Fisher's Exact
Parameter estimate	Odds ratio (OR)
Point estimate	12.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.85
upper limit	108.3

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[7]
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:

[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: 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

Statistical analysis title	Fisher's Exact
Statistical analysis description:	
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	< 0.0001
Method	Fisher's Exact
Parameter estimate	Odds ratio (OR)
Point estimate	19.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.02
upper limit	822.2

Secondary: Percentage of Participants with HBV DNA Undetectable at 24 Weeks After EOT/POP in Groups A and B

End point title	Percentage of Participants with HBV DNA Undetectable at 24 Weeks After EOT/POP in Groups A and B[8]
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)	

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: 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%)	16.8 (10.12 to 25.58)	2 (0.05 to 10.65)		

Statistical analyses

Statistical analysis title	Fisher's Exact
Statistical analysis description:	
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	= 0.0069
Method	Fisher's Exact
Parameter estimate	Odds ratio (OR)
Point estimate	9.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.45
upper limit	422.7

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[9]

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:

[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: 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

Statistical analysis title	Fisher's Exact
Statistical analysis description:	
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	= 0.0025
Method	Fisher's Exact
Parameter estimate	Odds ratio (OR)
Point estimate	7.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.61
upper limit	64.02

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[10]
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:

[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: 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 28.91)	2 (0.05 to 10.65)		

Statistical analyses

Statistical analysis title	Fisher's Exact
Statistical analysis description:	
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	= 0.0021
Method	Fisher's Exact
Parameter estimate	Odds ratio (OR)
Point estimate	12.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.8
upper limit	511.5

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[11]
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:

[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: 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

Statistical analysis title	Fisher's Exact

Statistical analysis description:

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	= 1
Method	Fisher's Exact
Parameter estimate	Odds ratio (OR)
Point estimate	1.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	8.23

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[12]

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:

[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: 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

Statistical analysis title	Fisher's Exact

Statistical analysis description:

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	= 0.7515
Method	Fisher's Exact
Parameter estimate	Odds ratio (OR)
Point estimate	1.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.36
upper limit	9.19

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[13]

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:

[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: 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

Statistical analysis title	Fisher's Exact
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	= 0.096
Method	Fisher's Exact

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[14]

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:

[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: 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

Statistical analysis title	Fisher's Exact
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	= 0.0163
Method	Fisher's Exact

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[15]

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:

[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: 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

Statistical analysis title	Fisher's Exact

Statistical analysis description:

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	= 0.6684
Method	Fisher's Exact
Parameter estimate	Odds ratio (OR)
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	2.11

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[16]

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:

[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: 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

Statistical analysis title	Fisher's Exact

Statistical analysis description:

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	= 0.0019
Method	Fisher's Exact
Parameter estimate	Odds ratio (OR)
Point estimate	4.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.58
upper limit	13.23

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[17]

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:

[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: 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

Statistical analysis title	Fisher's Exact

Statistical analysis description:

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	< 0.0001
Method	Fisher's Exact
Parameter estimate	Odds ratio (OR)
Point estimate	21.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.33
upper limit	902.1

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[18]

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:

[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: 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

Statistical analysis title	Fisher's Exact
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	= 0.0004
Method	Fisher's Exact

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[19]

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:

[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: 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)	6 (1.25 to 16.55)		

Statistical analyses

Statistical analysis title	Fisher's Exact

Statistical analysis description:

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	= 1
Method	Fisher's Exact
Parameter estimate	Odds ratio (OR)
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.25
upper limit	7.3

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[20]

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:

[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: 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

Statistical analysis title	Fisher's Exact
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	= 0.096
Method	Fisher's Exact

Secondary: Quantitative Serum ALT Level in Groups A and B

End point title	Quantitative Serum ALT Level in Groups A and B[21]

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:

[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: 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[22]

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:

[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: 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[23]

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:

[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: 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[24]

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:

[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: 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 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[25]

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:

[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: 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 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[26]

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:

[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: 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[27]

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:

[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: 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[28]

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:

[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: 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[29]

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:

[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: 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[30]

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:

[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: 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[31]

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:

[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: 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[32]

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:

[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: 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 HBeAg Seroconversion at EOT in Group C

End point title	Percentage of Participants with HBeAg Seroconversion at EOT

	in Group C[33]

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:

[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: 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 Loss of HBeAg at EOT in Group C

End point title	Percentage of Participants with Loss of HBeAg at EOT in Group C[34]

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:

[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: 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[35]

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:

[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: 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 Loss of HBsAg at EOT in Group C

End point title	Percentage of Participants with Loss of HBsAg at EOT in Group C[36]

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:

[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: 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:

[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: 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 <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[38]

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:

[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: 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[39]

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:

[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: 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[40]

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:

[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: 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[41]

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:

[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: 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[42]

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:

[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: 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[43]

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:

[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: 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[44]

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:

[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: 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[45]

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:

[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: 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[46]

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)

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: The substudy data were reported side-by-side for Groups A, B, and C.

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[47]

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)

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: The substudy data were planned to be analyzed for all groups combined.

End point values	All Groups Combined			
Subject group type	Reporting group			
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[48]

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:

[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: 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[49]

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:

[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: 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[50]

End point description:

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

End point type	Secondary

End point timeframe:

Weeks 12, 24, 48; FU Week 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: 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 12	10			
Week 24	10			
Week 48	10			
FU Week 24	10			

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Participants with >15% Drop in Weight Percentile for Age in Group C[51]

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:

[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: 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[52]

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:

[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: 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[53]

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:

[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: 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)	-0.041 (± 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[54]

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:

[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: 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[55]

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:

[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: 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[56]

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:

[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: 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[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). 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:

[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: 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[58]

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:

[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: 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[59]

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:

[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: 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[60]

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:

[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: 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[61]

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:

[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: 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[62]

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:

[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: 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[63]

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:

[63] - 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: 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:

[64] - 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: 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	9			
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[65]

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:

[65] - 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: 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:

[66] - 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: 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

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. Because participants could switch from Group B to Group D for up to 1 year following the Week 48 visit, not all participants had reached FU Week 24 at time of analysis.

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			

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	1 / 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	1 / 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	1 / 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		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 33 (6.06%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Nephropathy			

subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Osteochondrosis			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Hepatitis B			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Latent tuberculosis			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Microsporum infection			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tonsillitis			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	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
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
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
Epistaxis			
subjects affected / exposed	8 / 101 (7.92%)	0 / 49 (0.00%)	2 / 10 (20.00%)
occurrences (all)	8	0	2
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
Psychiatric disorders			
Irritability			
subjects affected / exposed	1 / 101 (0.99%)	0 / 49 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	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
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
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
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
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
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
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
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
Peritonsillar abscess			
subjects affected / exposed	1 / 101 (0.99%)	0 / 49 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	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
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		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 33 (63.64%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 33 (12.12%)		
occurrences (all)	8		
Fatigue			
subjects affected / exposed	3 / 33 (9.09%)		
occurrences (all)	3		
Influenza like illness			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Injection site pain			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	13 / 33 (39.39%)		
occurrences (all)	35		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Epistaxis			

subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Oropharyngeal pain			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Psychiatric disorders			
Irritability			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Body temperature increased			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	3		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	11 / 33 (33.33%)		
occurrences (all)	14		
Blood and lymphatic system disorders			
Neutropenia			

subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 33 (12.12%)		
occurrences (all)	6		
Nausea			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Pruritus			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Pain in extremity			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 33 (9.09%)		
occurrences (all)	4		
Oral herpes			
subjects affected / exposed	0 / 33 (0.00%)		
occurrences (all)	0		

Peritonsillar abscess subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Viral infection subjects affected / exposed occurrences (all)	 0 / 33 (0.00%) 0 0 / 33 (0.00%) 0 0 / 33 (0.00%) 0		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 1 / 33 (3.03%) 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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Results presented above include final analyses of the primary endpoint and most secondary endpoints. Group D had not reached FU Week 24 at time of analysis, so basic safety data were reported. New/updated data will be reported in the final results.

Notes: