Clinical trial results:
A Phase 2, Open-label, Single-arm, Multicenter Study to Assess Efficacy, Safety, Tolerability, and Pharmacokinetics of Treatment With JNJ-73763989, JNJ-56136379, Nucleos(t)ide Analogs, and Pegylated Interferon Alpha-2a in Virologically Suppressed Patients With Chronic Hepatitis B Virus Infection

Summary

EudraCT number	2020-003956-34
Trial protocol	PL
Global end of trial date	17 April 2023

Results information

Result version number	v1 (current)
This version publication date	02 May 2024
First version publication date	02 May 2024

Trial information

Trial identification

Sponsor protocol code	73763989PAHPB2006

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04667104
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development, LLC
Sponsor organisation address	920 US Highway 202, Raritan, NJ, United States, 08869-1420
Public contact	Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	17 April 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 April 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to assess efficacy and safety of a treatment regimen of JNJ-73763989 (JNJ-3989), JNJ-56136379 (JNJ-6379), and Nucleos(t)ide Analogs (NA) for 24 weeks with addition of Pegylated Interferon Alpha-2aNA (PegIFN-alpha2a) for 24 weeks.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 February 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 5
Country: Number of subjects enrolled	New Zealand: 4
Country: Number of subjects enrolled	Poland: 14
Country: Number of subjects enrolled	Taiwan: 25
Worldwide total number of subjects	48
EEA total number of subjects	14

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	48

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

At Week 12, subjects were assessed for PegIFN-alpha2a (PegIFN-alpha 2a) eligibility criteria & those who did not meet the criteria continued in Treatment Period 1 (TP 1) until Week 24 and those who met the criteria entered Treatment Period 2 (TP 2). After Week 12, one subject continued with TP1 regimen during TP2 until Week 24.

Period 1

Period 1 title	TP 1: From Week 1 to Week 12
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA

Arm description:

Subjects received JNJ-73763989 (JNJ-3989) 200 milligrams (mg) as a subcutaneous injection (SC) every 4 weeks (Q4W) along with JNJ-56136379 (JNJ-6379) 250 mg tablet once daily (QD) and nucleos(t)ide analog (NA) treatment (either entecavir [ETV] 0.5 mg, tenofovir disoproxil fumarate [TDF] 245 mg, or tenofovir alafenamide [TAF] 25 mg) QD up to 12 weeks in TP 1. Subjects enrolled until Protocol Amendment 3, also received single dose of JNJ-6379 250 mg orally as part of their study intervention. Subjects enrolled after Protocol Amendment 3, received JNJ-3989 + PegIFN-alpha 2a + NA only. Subjects were assessed for eligibility criteria for PegIFN-alpha 2a at Week 12 and those who met the criteria entered TP 2.

Arm type	Experimental
Investigational medicinal product name	JNJ-73763989
Investigational medicinal product code	
Other name	JNJ-3989
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received a single dose of JNJ-73763989 200 mg administered as SC injection in abdomen Q4W up to 12 weeks.

Investigational medicinal product name	JNJ-56136379
Investigational medicinal product code	
Other name	JNJ-6379
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received a single dose of JNJ-56136379 250 mg tablets administered orally up to 12 weeks.

Investigational medicinal product name	Nucleos(t)ide analog (NA)-Entecavir (ETV)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received a single dose of ETV 0.5 mg film-coated tablets administered orally up to 12 weeks.

Investigational medicinal product name	Nucleos(t)ide analog (NA)-Tenofovir alafenamide (TAF)
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received a single dose of TAF 25 mg film-coated tablets administered orally up to 12 weeks.

Investigational medicinal product name	Nucleos(t)ide analog (NA)-Tenofovir disoproxil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received a single dose of tenofovir disoproxil 245 mg film-coated tablets administered orally up to 12 weeks.

Number of subjects in period 1	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA
Started	48
Completed	48

Period 2

Period 2 title	TP 2: From Week 12 to Week 24
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA

Arm description:

Subjects who met the eligibility criteria for PegIFN-alpha2a (subjects who did not have disorders including but not limited to: autoimmune disorders, bone marrow suppression, hypoglycemia, hyperglycemia, diabetes mellitus) at Week 12 received combination treatment with JNJ-73763989 200 mg SC injection Q4W along with NA treatment (either ETV 0.5 mg, TDF 245 mg, or TAF 25 mg), QD up to Week 24 plus PegIFN-alpha 2a 180 micrograms (mcg) once weekly (Q1W) during TP 2. Subjects enrolled until Protocol Amendment 3, also received single dose of JNJ-6379 250 mg orally as part of their study intervention. Subjects enrolled after Protocol Amendment 3, received JNJ-3989 + PegIFN-alpha 2a + NA only.

Arm type	Experimental
Investigational medicinal product name	JNJ-73763989
Investigational medicinal product code	
Other name	JNJ-3989
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

From Week 12, subjects received a single dose of JNJ-73763989 200 mg administered as SC injection in abdomen Q4W up to 12 weeks.

Investigational medicinal product name	PegIFN-alpha2a
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

From Week 12, subjects received a single dose of PegIFN-alpha2a 180 mcg QW administered as SC injection in the thigh or abdomen for 12 weeks.

Investigational medicinal product name	Nucleos(t)ide analog (NA)-ETV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

From Week 12, subjects received a single dose of 0.5 mg ETV film-coated tablets administered orally up to 12 weeks.

Investigational medicinal product name	Nucleos(t)ide analog (NA)-Tenofovir disoproxil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

From Week 12, subjects received a single dose of 245 mg tenofovir disoproxil film-coated tablets administered orally up to 12 weeks.

Investigational medicinal product name	Nucleos(t)ide analog (NA)-TAF
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

From Week 12, subjects received a single dose of 25 mg TAF film-coated tablets administered orally up to 12 weeks.

Investigational medicinal product name	JNJ-56136379
Investigational medicinal product code	
Other name	JNJ-6379
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

From Week 12, subjects received a single dose of JNJ-56136379 250 mg tablets administered orally up to 12 weeks.

Number of subjects in period 2	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA
Started	48
Completed	48

Period 3

Period 3 title	Follow-Up Period: From Week 24 - Week 72
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Follow-Up (FU) Period-nucleos(t)ide analog (NA)

Arm description:

At Week 24, prior to follow-up period, all subjects stopped treatment with JNJ-73763989 + JNJ-56136379 + PegIFN-alpha2a. Subjects who met the protocol-defined NA treatment completion criteria (hepatitis B surface antigen [HBsAg] <10 international units/millilitre [IU/mL], and hepatitis B e antigen [HBeAg]-negative, and hepatitis B virus deoxyribonucleic acid [HBV DNA] <lower limit of quantification [LLOQ], and alanine aminotransferase [ALT] <3*Upper limit of normal [ULN]) at Week 24, stopped NA at Week 26 (that is follow up Week 2). Subjects who did not meet NA completion criteria continued NA treatment during the follow-up period up to Week 72 (that is, follow-up Week 48).

Arm type	Experimental
Investigational medicinal product name	Nucleos(t)ide analog (NA)-Tenofovir disoproxil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

At Week 24, subjects received a single dose of tenofovir disoproxil 245 mg film-coated tablets administered orally up to 48 weeks.

Investigational medicinal product name	Nucleos(t)ide analog (NA)-ETV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

At Week 24, subjects received a single dose of ETV 0.5 mg film-coated tablets administered orally up to 48 weeks.

Investigational medicinal product name	Nucleos(t)ide analog (NA)-TAF
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

At Week 24, subjects received a single dose of TAF 25 mg film-coated tablets administered orally up to 48 weeks.

Number of subjects in period 3	Follow-Up (FU) Period-nucleos(t)ide analog (NA)
Started	48
Completed	47
Not completed	1
Unspecified	1

Baseline characteristics

Reporting groups

Reporting group title	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA

Reporting group description:

Subjects received JNJ-73763989 (JNJ-3989) 200 milligrams (mg) as a subcutaneous injection (SC) every 4 weeks (Q4W) along with JNJ-56136379 (JNJ-6379) 250 mg tablet once daily (QD) and nucleos(t)ide analog (NA) treatment (either entecavir [ETV] 0.5 mg, tenofovir disoproxil fumarate [TDF] 245 mg, or tenofovir alafenamide [TAF] 25 mg) QD up to 12 weeks in TP 1. Subjects enrolled until Protocol Amendment 3, also received single dose of JNJ-6379 250 mg orally as part of their study intervention. Subjects enrolled after Protocol Amendment 3, received JNJ-3989 + PegIFN-alpha 2a + NA only. Subjects were assessed for eligibility criteria for PegIFN-alpha 2a at Week 12 and those who met the criteria entered TP 2.

Reporting group values	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA	Total	
Number of subjects	48	48	
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	48	48	
From 65 to 84 years	0	0	
85 years and over	0	0	
Title for AgeContinuous Units: years			
arithmetic mean	44.6		
standard deviation	± 1.47	-	
Title for Gender Units: subjects			
Female	8	8	
Male	40	40	

End points reporting groups

Reporting group title	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA

Reporting group description:

Subjects received JNJ-73763989 (JNJ-3989) 200 milligrams (mg) as a subcutaneous injection (SC) every 4 weeks (Q4W) along with JNJ-56136379 (JNJ-6379) 250 mg tablet once daily (QD) and nucleos(t)ide analog (NA) treatment (either entecavir [ETV] 0.5 mg, tenofovir disoproxil fumarate [TDF] 245 mg, or tenofovir alafenamide [TAF] 25 mg) QD up to 12 weeks in TP 1. Subjects enrolled until Protocol Amendment 3, also received single dose of JNJ-6379 250 mg orally as part of their study intervention. Subjects enrolled after Protocol Amendment 3, received JNJ-3989 + PegIFN-alpha 2a + NA only. Subjects were assessed for eligibility criteria for PegIFN-alpha 2a at Week 12 and those who met the criteria entered TP 2.

Reporting group title	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA

Reporting group description:

Subjects who met the eligibility criteria for PegIFN-alpha2a (subjects who did not have disorders including but not limited to: autoimmune disorders, bone marrow suppression, hypoglycemia, hyperglycemia, diabetes mellitus) at Week 12 received combination treatment with JNJ-73763989 200 mg SC injection Q4W along with NA treatment (either ETV 0.5 mg, TDF 245 mg, or TAF 25 mg), QD up to Week 24 plus PegIFN-alpha 2a 180 micrograms (mcg) once weekly (Q1W) during TP 2. Subjects enrolled until Protocol Amendment 3, also received single dose of JNJ-6379 250 mg orally as part of their study intervention. Subjects enrolled after Protocol Amendment 3, received JNJ-3989 + PegIFN-alpha 2a + NA only.

Reporting group title	Follow-Up (FU) Period-nucleos(t)ide analog (NA)

Reporting group description:

At Week 24, prior to follow-up period, all subjects stopped treatment with JNJ-73763989 + JNJ-56136379 + PegIFN-alpha2a. Subjects who met the protocol-defined NA treatment completion criteria (hepatitis B surface antigen [HBsAg] <10 international units/millilitre [IU/mL], and hepatitis B e antigen [HBeAg]-negative, and hepatitis B virus deoxyribonucleic acid [HBV DNA] <lower limit of quantification [LLOQ], and alanine aminotransferase [ALT] <3*Upper limit of normal [ULN]) at Week 24, stopped NA at Week 26 (that is follow up Week 2). Subjects who did not meet NA completion criteria continued NA treatment during the follow-up period up to Week 72 (that is, follow-up Week 48).

Subject analysis set title	Pooled(JNJ-3989 200mg+JNJ-6379 250mg+PegIFN-alpha2a 180mcg+NA)
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects received JNJ-3989 200 mg as SC Q4W along with JNJ-6379 250 mg tablet QD and NA treatment (either ETV 0.5 mg, TDF 245 mg, or TAF 25 mg QD up to 12 weeks in TP1. At Week 12, subjects who met eligibility criteria for PegIFN-alpha 2a entered TP2. Subjects in TP2 received combination treatment of JNJ-3989 200 mg SC injection Q4W with NA treatment up to Week 24 plus PegIFN-alpha 2a 180 mcg Q1W. At Week 24, before follow-up period, subjects stopped JNJ-3989 + JNJ-6379 + PegIFN-alpha2a. At Week 26, those who met the NA treatment completion criteria stopped NA (follow up Week 2) and those who did not meet criteria continued NA treatment in follow-up period up to Week 72 (follow-up Week 48). Subjects enrolled until Protocol Amendment 3 (PA3), also received JNJ-6379 250 mg orally as intervention in TP1 and TP2 and those enrolled after PA3, received only JNJ-3989 + PegIFN alpha 2a + NA only during study.

Primary: Percentage of Subjects with a Reduction of at Least 2 log10 International Unit/millilitres (IU/mL) in Hepatitis B Surface Antigen (HBsAg) Levels From Baseline (Day 1) to Week 24

End point title	Percentage of Subjects with a Reduction of at Least 2 log10 International Unit/millilitres (IU/mL) in Hepatitis B Surface Antigen (HBsAg) Levels From Baseline (Day 1) to Week 24[1]

End point description:

Percentage of subjects with a reduction of at least 2 log10IU/mL in HBsAg levels from baseline to Week 24 were reported. A responder was defined as a subject with reduction of at least 2 log10 IU/mL in HBsAg levels from Baseline at Week 24. Full Analysis Set (FAS) included all subjects who were enrolled and who received at least 1 dose of study intervention within this intervention-specific appendix (ISA). Data for this endpoint was planned to be collected and analyzed for specified arm only.

End point type	Primary

End point timeframe:

Baseline (Day 1) to Week 24

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical testing was planned. Only descriptive analysis was performed.

End point values	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: percentage of subjects				
number (confidence interval 90%)	64.6 (51.73 to 76.02)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Clinically Significant Abnormalities in Vital Signs as a Measure of Safety and Tolerability

End point title	Number of Subjects with Clinically Significant Abnormalities in Vital Signs as a Measure of Safety and Tolerability

End point description:

Number of subjects with clinically significant abnormalities in vital signs (pulse rate, and blood pressure [systolic and diastolic]) were reported. Safety analysis set included all subjects who received at least 1 dose of study intervention. Subjects were analyzed according to the study intervention they actually received.

End point type	Secondary

End point timeframe:

Treatment Period 1: From Baseline (Day 1) up to Week 12; Treatment Period 2: From Week 12 up to Week 24; Follow-Up: From Week 24 up to Week 72

End point values	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA	Follow-Up (FU) Period-nucleos(t)ide analog (NA)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	48	48	
Units: subjects	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Treatment Emergent Serious Adverse Events (SAEs) as a Measure of Safety and Tolerability

End point title	Percentage of Subjects with Treatment Emergent Serious Adverse Events (SAEs) as a Measure of Safety and Tolerability

End point description:

An AE is any untoward medical occurrence in a subject participating in a clinical study that does not necessarily have a causal relationship with the pharmaceutical/biological agent under study. TEAEs were AEs with onset during the intervention period or follow-up period or that were a consequence of a pre-existing condition that had worsened since baseline. A SAE is an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Safety analysis set included all subjects who received at least 1 dose of study intervention. Subjects were analyzed according to the study intervention they actually received.

End point type	Secondary

End point timeframe:

Treatment Period 1: From Baseline (Day 1) up to Week 12; Treatment Period 2: From Week 12 up to Week 24; Follow-Up: From Week 24 up to Week 72

End point values	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA	Follow-Up (FU) Period-nucleos(t)ide analog (NA)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	48	48	
Units: percentage of subjects				
number (not applicable)	0	2.1	8.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Treatment Emergent Adverse Events (TEAEs) as a Measure of Safety and Tolerability

End point title	Percentage of Subjects with Treatment Emergent Adverse Events (TEAEs) as a Measure of Safety and Tolerability

End point description:

Percentage of subjects with TEAEs were reported. An adverse event (AE) was any untoward medical occurrence in a subject participating in a clinical study that does not necessarily have a causal relationship with the pharmaceutical/biological agent under study. TEAEs were AEs with onset during the intervention period or follow-up period or that were a consequence of a pre-existing condition that had worsened since baseline. Safety analysis set included all subjects who received at least 1 dose of study intervention. Subjects were analyzed according to the study intervention they actually received.

End point type	Secondary

End point timeframe:

Treatment Period 1: From Baseline (Day 1) up to Week 12; Treatment Period 2: From Week 12 up to Week 24; Follow-Up: From Week 24 up to Week 72

End point values	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA	Follow-Up (FU) Period-nucleos(t)ide analog (NA)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	48	48	
Units: percentage of subjects				
number (not applicable)	52.1	87.5	60.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Clinically Significant Abnormalities in Laboratory Findings as a Measure of Safety and Tolerability

End point title	Number of Subjects with Clinically Significant Abnormalities in Laboratory Findings as a Measure of Safety and Tolerability

End point description:

Number of subjects with clinically significant abnormalities in laboratory findings (including hematology, blood biochemistry, and urinalysis) were reported. Only parameters in which any subject had abnormality are reported below. Safety analysis set included all subjects who received at least 1 dose of study intervention. Subjects were analyzed according to the study intervention they actually received. Here "N" signifies the number of subjects that were evaluable for this endpoint and "n"(number of subjects analyzed) signifies number of subjects analyzed at specified timepoints.

End point type	Secondary

End point timeframe:

Treatment Period 1: From Baseline (Day 1) up to Week 12; Treatment Period 2: From Week 12 up to Week 24; Follow-Up: From Week 24 up to Week 72

End point values	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA	Follow-Up (FU) Period-nucleos(t)ide analog (NA)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	48	48	
Units: subjects				
Treatment-emergent (TE)-Grade 3 ALT elevations	1	1	1	
TE-Grade 3 total bilirubin elevations	0	0	1	
TE-Grade 3 direct bilirubin elevations	0	0	2	
Treatment-emergent-High serum indirect bilirubin	0	0	3	
Renal complications-eGFR Decreases	0	0	0	

Hematology-low absolute neutrophil count Grade 1	1	13	2	
Hematology-low absolute neutrophil count Grade 2	0	2	1	
Hematology-low absolute neutrophil count Grade 3	0	3	0	
Hematology-low absolute neutrophil count Grade 4	0	1	0	
Hematology-low absolute lymphocyte count Grade 1	1	1	0	
Hematology-low absolute lymphocyte count Grade 2	1	3	0	
Hematology-low absolute lymphocyte count Grade 3	0	3	2	
Hematology-low absolute lymphocyte count Grade 4	0	1	1	
Hematology-decreased platelets of Grade 1	0	20	8	
Hematology-decreased platelets of Grade 2	0	5	0	
Hematology-low hemoglobin Grade 2	0	0	1	
Hematology-low WBC count of Grade 1	0	14	5	
Hematology-low WBC count of Grade 2	0	6	1	
Hematology-low WBC count of Grade 3	0	2	0	
Chemistry-LDL cholesterol Grade 3	2	1	2	
Chemistry-eGFR creatinine low Grade 3 elevation	1	0	0	
Chemistry-eGFR Cystatin C low Grade 3 elevation	0	1	2	
Chemistry-Grade 3 elevations in triglycerides	0	2	0	
Chemistry-Grade 3 elevation amylase	0	0	1	
Chemistry-Grade 3 elevation direct bilirubin high	0	0	2	
Chemistry-lipaseGrade 4 elevation	0	0	1	
Urinalysis-Grade 1 glycosuria (n=0, 0, 24)	0	0	1	
Urinalysis-Grade 1 hematuria (n=0, 17, 18)	0	1	1	
Urinalysis-Grade 2 hematuria (n=10, 17, 18)	1	1	1	
Urinalysis-Grade 1 proteinuria (n=19, 23, 24)	2	5	4	
Urinalysis-Grade 2 proteinuria (n=19, 23, 24)	1	1	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with HBsAg Levels Below Different Cut-offs

End point title	Percentage of Subjects with HBsAg Levels Below Different Cut-offs

End point description:

Percentage of subjects with HBsAg levels below different cut-offs were reported. The cut-offs for HBsAg levels were as followed: <1000 IU/mL, <100 IU/mL, <10 IU/mL, <1 IU/mL, <LLOQ (0.05 IU/mL). FAS

included all subjects who were enrolled and who received at least 1 dose of study intervention within this ISA.

End point type	Secondary

End point timeframe:

Treatment Period 1: From Baseline (Day 1) up to Week 12; Treatment Period 2: From Week 12 up to Week 24; Follow-Up: From Week 24 up to Week 72

End point values	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA	Follow-Up (FU) Period-nucleos(t)ide analog (NA)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	48	48	
Units: percentage of subjects				
number (not applicable)				
<LLOQ (0.05 IU/mL)	0	2.1	2.1	
<1 IU/mL	4.2	6.3	2.1	
<10 IU/mL	12.5	47.9	4.2	
<100 IU/mL	58.3	91.7	27.1	
<1000 IU/mL	89.6	97.9	68.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Meeting the Protocol-defined Nucleos(t)ide Analog (NA) Treatment Completion Criteria at End of Study Intervention (EOSI)

End point title	Percentage of Subjects Meeting the Protocol-defined Nucleos(t)ide Analog (NA) Treatment Completion Criteria at End of Study Intervention (EOSI)

End point description:

Percentage of subjects meeting the protocol-defined NA treatment completion criteria at EOSI were reported. NA treatment completion criteria defined based on laboratory results at Week 24 were; HBsAg <10 IU/mL; HBeAg-negative; HBV DNA <20 IU/mL, that is, lower limit of quantification (LLOQ); alanine aminotransferase (ALT) <3* Upper Limit of Normal (ULN). FAS included all subjects who were enrolled and who received at least 1 dose of study intervention within this ISA. Data for this endpoint was not planned to be collected and analyzed for Treatment Period 1 and Follow-Up period as pre-specified in protocol.

End point type	Secondary

End point timeframe:

At Week 24 (EOSI)

End point values	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: percentage of subjects				
number (not applicable)	31.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Clinically Significant Abnormalities in Ophthalmic Examination as a Measure of Safety and Tolerability

End point title	Number of Subjects with Clinically Significant Abnormalities in Ophthalmic Examination as a Measure of Safety and Tolerability

End point description:

Number of subjects with clinically significant abnormalities in ophthalmic examination were planned to be reported. Safety analysis set included all subjects who received at least 1 dose of study intervention. Subjects were analyzed according to the study intervention they actually received. Data for this endpoint was planned to be collected and analyzed in TP 1 and TP 2 for participants with diabetes/hypertension only. Since no subject had diabetes/hypertension, data for this endpoint was not collected and analyzed.

End point type	Secondary

End point timeframe:

Treatment Period 1: From Baseline (Day 1) up to Week 12; Treatment Period 2: From Week 12 up to Week 24

End point values	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: subjects				

Notes:

[2] - Data was planned to be collected for subjects at risk factor of diabetes or hypertension only.

[3] - Data was planned to be collected for subjects at risk factor of diabetes or hypertension only.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Clinically Significant Abnormalities in Physical Examination as a Measure of Safety and Tolerability

End point title	Number of Subjects with Clinically Significant Abnormalities in

	Physical Examination as a Measure of Safety and Tolerability

End point description:

Number of subjects with clinically significant abnormalities in physical examination were reported. Safety analysis set included all subjects who received at least 1 dose of study intervention. Subjects were analyzed according to the study intervention they actually received. Data for this outcome measure was not planned to be collected and analyzed for Follow-Up Period as pre-specified in protocol.

End point type	Secondary

End point timeframe:

Treatment Period 1: From Baseline (Day 1) up to Week 12; Treatment Period 2: From Week 12 up to Week 24

End point values	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	48		
Units: subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Clinically Significant Abnormalities in 12-Lead Electrocardiogram (ECGs) as a Measure of Safety and Tolerability

End point title	Number of Subjects with Clinically Significant Abnormalities in 12-Lead Electrocardiogram (ECGs) as a Measure of Safety and Tolerability

End point description:

Number of subjects with clinically significant abnormalities in 12- lead ECGs (heart rate, PR, QRS and QT corrected [QTc]) were reported. Safety analysis set included all subjects who received at least 1 dose of study intervention. Subjects were analyzed according to the study intervention they actually received.

End point type	Secondary

End point timeframe:

Treatment Period 1: From Baseline (Day 1) up to Week 12; Treatment Period 2: From Week 12 up to Week 24; Follow-Up: From Week 24 up to Week 28

End point values	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA	Follow-Up (FU) Period-nucleos(t)ide analog (NA)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	48	48	
Units: subjects	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with HBeAg Levels Below Different Cut-offs

End point title	Percentage of Subjects with HBeAg Levels Below Different Cut-offs

End point description:

Percentage of subjects with HBeAg levels below different cut-offs were reported. The cut-offs for HBeAg levels were as followes:< 100 IU/mL, < 10 IU/mL, < 1 IU/mL, < LLOQ (0.11 IU/mL). FAS included all subjects who were enrolled and who received at least 1 dose of study intervention within this ISA. Here "N" (Number of subjects that started the Arm) signifies the number of subjects that were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Treatment Period 1: From Baseline (Day 1) up to Week 12; Treatment Period 2: From Week 12 up to Week 24; Follow-Up: From Week 24 up to Week 72

End point values	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA	Follow-Up (FU) Period-nucleos(t)ide analog (NA)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	11	11	
Units: percentage of subjects				
number (not applicable)				
< LLOQ (0.11 IU/mL)	36.4	27.3	27.3	
< 1 IU/mL	90.9	100.0	81.8	
< 10 IU/mL	100.0	100.0	100.0	
< 100 IU/mL	100.0	100.0	100.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Hepatitis B Virus (HBV) Deoxyribonucleic Acid (DNA) Levels Below different Cut-offs

End point title	Percentage of Subjects with Hepatitis B Virus (HBV) Deoxyribonucleic Acid (DNA) Levels Below different Cut-offs

End point description:

Percentage of subjects with HBV DNA levels below cut-offs were reported. The cut-offs for HBV DNA were as followed: <LLOQ(=20 IU/mL) for target detected and not detected, < LLOQ for target not

detected, < LLOQ for target detected, <60 IU/mL, <100 IU/mL, <200 IU/mL, <1000 IU/mL, <2000 IU/mL, <20000 IU/mL. FAS included all subjects who were enrolled and who received at least 1 dose of study intervention within this ISA.

End point type	Secondary

End point timeframe:

Treatment Period 1: From Baseline (Day 1) up to Week 12; Treatment Period 2: From Week 12 up to Week 24; Follow-Up: From Week 24 up to Week 72

End point values	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA	Follow-Up (FU) Period-nucleos(t)ide analog (NA)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	48	48	
Units: percentage of subjects				
number (not applicable)				
< LLOQ for target detected and not detected	95.8	75.0	81.3	
< LLOQ for target not detected	52.1	27.1	54.2	
< LLOQ for target detected	43.8	47.9	27.1	
< 60 IU/mL	100.0	89.6	83.3	
< 100 IU/mL	100.0	95.8	83.3	
< 200 IU/mL	100.0	97.9	85.4	
< 1000 IU/mL	100.0	100.0	89.6	
< 2000 IU/mL	100.0	100.0	93.8	
< 20000 IU/mL	100.0	100.0	97.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with HBsAg Seroconversion

End point title	Percentage of Subjects with HBsAg Seroconversion

End point description:

Percentage of subjects with HBsAg seroconversion were reported. Seroconversion of HBsAg is defined as having achieved HBsAg seroclearance (defined as HBsAg <LLOQ [0.05 IU/mL]) and appearance of anti-HBs antibodies. FAS included all subjects who were enrolled and who received at least 1 dose of study intervention within this ISA. Here "N" (Number of subjects that started the Arm) signifies the number of subjects that were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Treatment Period 1: From Baseline (Day 1) up to Week 12; Treatment Period 2: From Week 12 up to Week 24; Follow-Up: From Week 24 up to Week 72

End point values	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA	Follow-Up (FU) Period-nucleos(t)ide analog (NA)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	45	46	46	
Units: percentage of subjects				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with HBeAg Seroconversion

End point title	Percentage of Subjects with HBeAg Seroconversion

End point description:

Percentage of subjects with HBeAg seroconversion were reported. Seroconversion of HBeAg was defined as having achieved HBeAg seroclearance (as HBeAg level <LLOQ [0.11 IU/mL]) and appearance of anti-HBe antibodies, defined as baseline anti-HBe antibodies with a negative result and a post-baseline assessment with positive result. FAS included all subjects who were enrolled and who received at least 1 dose of study intervention within this ISA. Here "N" (Number of subjects that started the Arm) signifies the number of subjects that were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Treatment Period 1: From Baseline (Day 1) up to Week 12; Treatment Period 2: From Week 12 up to Week 24; Follow-Up: From Week 24 up to Week 72

End point values	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA	Follow-Up (FU) Period-nucleos(t)ide analog (NA)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	11	11	
Units: percentage of subjects				
number (not applicable)	0	10.0	20.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with ALT Levels Greater Than or Equal to (>=) 3*ULN

End point title	Percentage of Subjects with ALT Levels Greater Than or Equal to (>=) 3*ULN

End point description:

Percentage of subjects with ALT levels >=3*ULN were reported. FAS included all subjects who were enrolled and who received at least 1 dose of study intervention within this ISA. Here "N" (Number of subjects that started the Arm) signifies the number of subjects that were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Treatment Period 1: From Baseline (Day 1) up to Week 12; Treatment Period 2: From Week 12 up to Week 24; Follow-Up: From Week 24 up to Week 72

End point values	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA	Follow-Up (FU) Period-nucleos(t)ide analog (NA)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	3	
Units: percentage of subjects				
number (not applicable)	33.3	33.3	66.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline Over Time in HBsAg Levels

End point title	Change from Baseline Over Time in HBsAg Levels

End point description:

Change from baseline over time in HBsAg levels were reported. The baseline assessment was defined as the last observed non-missing measurement before the date and time of the first administration of any of study agent. FAS included all subjects who were enrolled and who received at least 1 dose of study intervention within this ISA.

End point type	Secondary

End point timeframe:

Treatment Period 1: From Baseline (Day 1) up to Week 12; Treatment Period 2: From Baseline (Day 1) up to Week 24; Follow-Up: From Baseline (Day 1) up to Week 72

End point values	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA	Follow-Up (FU) Period-nucleos(t)ide analog (NA)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	48	48	
Units: log10 IU/mL				
arithmetic mean (standard error)	-1.43 (± 0.070)	-2.18 (± 0.084)	-0.71 (± 0.092)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline Over Time in HBV DNA Levels

End point title	Change from Baseline Over Time in HBV DNA Levels

End point description:

Change from baseline over time in HBV DNA levels were reported. The baseline assessment was defined as the last observed non-missing measurement before the date and time of the first administration of any of study agent. FAS included all subjects who were enrolled and who received at least 1 dose of study intervention within this ISA.

End point type	Secondary

End point timeframe:

Treatment Period 1: From Baseline (Day 1) up to Week 12; Treatment Period 2: From Baseline (Day 1) up to Week 24; Follow-Up: From Baseline (Day 1) up to Week 72

End point values	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA	Follow-Up (FU) Period-nucleos(t)ide analog (NA)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	48	48	
Units: log10 IU/mL				
arithmetic mean (standard error)	0.03 (± 0.032)	0.28 (± 0.059)	0.36 (± 0.145)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline Over Time in HBeAg Levels

End point title	Change from Baseline Over Time in HBeAg Levels

End point description:

Change from baseline over time in HBeAg levels were reported. The baseline assessment was defined as the last observed non-missing measurement before the date and time of the first administration of any of study agent. FAS included all subjects who were enrolled and who received at least 1 dose of study intervention within this ISA. Here "N" (Number of subjects analyzed) signifies the number of subjects that were evaluable for this endpoint and "n"(number analyzed) signifies number of subjects analysed at specified categories.

End point type	Secondary

End point timeframe:

Treatment Period 1: From Baseline (Day 1) up to Week 12; Treatment Period 2: From Baseline (Day 1) up to Week 24; Follow-Up: From Baseline (Day 1) up to Week 72

End point values	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA	Follow-Up (FU) Period-nucleos(t)ide analog (NA)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	11	11	
Units: log10 IU/mL				
arithmetic mean (standard error)	-0.68 (± 0.087)	-0.72 (± 0.106)	-0.53 (± 0.112)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Occurrence of HBsAg Seroclearance

End point title	Time to First Occurrence of HBsAg Seroclearance

End point description:

Time to first occurrence of HBsAg seroclearance were reported in median time. Time to first occurrence of the HBsAg seroclearance was defined as the number of days between the date of first study intervention intake and the date of the first occurrence of the HBsAg seroclearance. FAS included all subjects who were enrolled and who received at least 1 dose of study intervention within this ISA. "9999" signifies that median and range was not estimable as at least 50% subjects did not reach HBsAg seroclearance. Data for this endpoint was planned to be collected and analysed in a single arm.

End point type	Secondary

End point timeframe:

From Baseline (Day 1) up to Week 72

End point values	Pooled(JNJ-3989 200mg+JNJ-6379 250mg+PegIFN-alpha2a 180mcg+NA)			
Subject group type	Subject analysis set			
Number of subjects analysed	48			
Units: weeks				
median (full range (min-max))	99999 (-99999 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with HBV DNA < LLOQ at Week 48 Without Re-starting NA Treatment

End point title	Percentage of Subjects with HBV DNA < LLOQ at Week 48 Without Re-starting NA Treatment

End point description:

Percentage of subjects with HBV DNA <LLOQ (20 IU/mL) at Week 48 (that is, 24 weeks after completion of all study interventions at Week 24) without re-starting NA treatment were reported. FAS included all subjects who were enrolled and who received at least 1 dose of study intervention within this ISA. Data for this outcome measure was planned to be collected and analyzed for Follow-Up Period only as pre-specified in protocol.

End point type	Secondary

End point timeframe:

At Week 48 (24 weeks after completion of all study interventions at Week 24)

End point values	Follow-Up (FU) Period-nucleos(t)ide analog (NA)			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: percentage of subjects				
number (not applicable)	81.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Occurrence of HBeAg Seroclearance

End point title	Time to First Occurrence of HBeAg Seroclearance

End point description:

Time to first occurrence of HBeAg seroclearance were reported in median time. Time to first occurrence of the HBeAg seroclearance is defined as the number of days between the date of first study intervention intake and the date of the first occurrence of the HBeAg seroclearance. FAS included all subjects who were enrolled and who received at least 1 dose of study intervention within this ISA. Data for this endpoint was planned to be collected and analysed in a single arm.

End point type	Secondary

End point timeframe:

From Baseline (Day 1) up to Week 72

End point values	Pooled(JNJ-3989 200mg+JNJ-6379 250mg+PegIFN-alpha2a 180mcg+NA)			
Subject group type	Subject analysis set			
Number of subjects analysed	48			
Units: weeks				
median (full range (min-max))	14.1 (4.1 to 72.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with HBsAg Seroclearance at Week 48 without re-starting NA treatment

End point title	Percentage of Subjects with HBsAg Seroclearance at Week 48 without re-starting NA treatment

End point description:

Proportion of subjects with HBsAg seroclearance at Week 48 (that is, 24 weeks after completion of all study interventions at Week 24) without re-starting NA treatment were reported. HBsAg seroclearance was defined as [quantitative] HBsAg <LLOQ (0.05 IU/mL). FAS included all subjects who were enrolled and who received at least 1 dose of study intervention within this ISA. Data for this outcome measure was planned to be collected and analyzed for Follow-Up Period as pre-specified in protocol.

End point type	Secondary

End point timeframe:

At Week 48 (24 weeks after completion of all study interventions at Week 24)

End point values	Follow-Up (FU) Period-nucleos(t)ide analog (NA)			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: percentage of subjects				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Virologic Breakthrough

End point title	Percentage of Subjects with Virologic Breakthrough

End point description:

Percentage of subjects with virologic breakthrough were reported. It was defined as confirmed on-treatment (the time period during which the subject receives any of the study treatments) HBV DNA

increase by >1 log10 IU/mL from nadir or confirmed on-treatment HBV DNA level >200 IU/mL in subjects who had HBV DNA level <LLOQ (20 IU/mL) of the HBV DNA assay. Confirmed means that the criteria was fulfilled at 2 or more consecutive time points or at the last observed time point. FAS included all subjects who were enrolled and who received at least 1 dose of study intervention within this ISA. Here "N" (Number of subjects that started the Arm) signifies the number of subjects that were evaluable for this endpoint and "n"(number of subjects analyzed) signifies number of subjects analyzed at specified categories.

End point type	Secondary

End point timeframe:

Treatment Period 1: From Baseline (Day 1) up to Week 12; Treatment Period 2: From Week 12 up to Week 24; Follow-Up: From Week 24 up to Week 72

End point values	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA	Follow-Up (FU) Period-nucleos(t)ide analog (NA)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	48	38	
Units: percentage of subjects				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Occurrence of HBV DNA < LLOQ

End point title	Time to First Occurrence of HBV DNA < LLOQ

End point description:

Time to first occurrence of HBV DNA < LLOQ (20 IU/mL) were reported in median time. Time to first occurrence of the HBV DNA < LLOQ is defined as the number of days between the date of first study intervention intake and the date of the first occurrence of the HBV DNA < LLOQ. FAS included all subjects who were enrolled and who received at least 1 dose of study intervention within this ISA. Data for this endpoint was planned to be collected and analysed in a single arm.

End point type	Secondary

End point timeframe:

From Baseline (Day 1) up to Week 72

End point values	Pooled(JNJ-3989 200mg+JNJ-6379 250mg+PegIFN-alpha2a 180mcg+NA)			
Subject group type	Subject analysis set			
Number of subjects analysed	48			
Units: weeks				
median (full range (min-max))	4.1 (2.9 to			

32.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) of JNJ-73763989 (JNJ-73763976 and JNJ-73763924)

End point title	Maximum Observed Plasma Concentration (Cmax) of JNJ-73763989 (JNJ-73763976 and JNJ-73763924)

End point description:

The maximum observed plasma concentrations (Cmax) of JNJ-73763989 (JNJ-73763976 and JNJ-73763924) were reported. Pharmacokinetics(PK) analysis set included all subjects who received at least 1 dose of study intervention and had at least 1 valid blood sample drawn for PK analysis. Here "N" (Number of subjects that started the Arm) signifies the number of subjects that were evaluable for this endpoint and "n"(number of subjects analyzed) signifies number of subjects analyzed at specified categories. Data for this endpoint was planned to be collected and analyzed for TP 1 and TP 2 only as specified in protocol.

End point type	Secondary

End point timeframe:

Treatment Period 1: Day 1 Week 1; Treatment Period 2: Day 1, Week 12

End point values	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: nanograms/milliliters (ng/mL)				
arithmetic mean (standard deviation)				
JNJ-73763976	1338 (± 971)	928 (± 692)		
JNJ-73763924	271 (± 197)	185 (± 130)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Biochemical Flares

End point title	Percentage of Subjects with Biochemical Flares

End point description:

Percentage of subjects with biochemical flares were reported. On-treatment biochemical flare was defined as confirmed ALT and/or AST >=3*ULN and >=3*nadir, while the subject received any of the study interventions. Off-treatment biochemical flare was defined as confirmed ALT and/or AST =3*ULN and =3*nadir, while the subject did not receive any of the study interventions (Off treatment, including

NA). FAS included all subjects who were enrolled and who received at least 1 dose of study intervention within this ISA. Here "N" (Number of subjects that started the Arm) signifies the number of subjects that were evaluable for this endpoint and "n"(number of subjects analyzed) signifies number of subjects analyzed at specified categories. Here "99999" signifies no participant were available for the analysis.

End point type	Secondary

End point timeframe:

Treatment Period 1: From Baseline (Day 1) up to Week 12; Treatment Period 2: From Week 12 up to Week 24; Follow-Up: From Week 24 up to Week 72

End point values	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA	Follow-Up (FU) Period-nucleos(t)ide analog (NA)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	48	38	
Units: percentage of subjects				
number (confidence interval 90%)				
On-Treatment (n=48, 48, 38)	0 (0 to 6.05)	4.2 (0.75 to 12.54)	0 (0 to 7.58)	
Off-Treatment (n=0, 0, 15)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	0 (0 to 0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Virologic Flares

End point title	Percentage of Subjects with Virologic Flares

End point description:

Percentage of subjects with virologic flares were reported. Virologic flare was defined as confirmed HBV DNA >peak threshold (lowest peak to qualify as virologic flare was HBV DNA >200 IU/mL) in subjects who were off-treatment. Off-treatment was defined as the time period after stopping all study treatments (including NA) and had HBV DNA <LLOQ (20 IU/mL) at the last observed time point on all study interventions. FAS included all subjects who were enrolled and who received at least 1 dose of study intervention within this ISA. Here "N" (Number of subjects that started the Arm) signifies the number of subjects that were evaluable for this endpoint and "n"(number of subjects analyzed) signifies number of subjects analyzed at specified categories. Data for this outcome measure was planned to be collected and analyzed for Follow-Up period only as pre-specified in protocol.

End point type	Secondary

End point timeframe:

Treatment Period 1: From Baseline (Day 1) up to Week 12; Treatment Period 2: From Week 12 up to Week 24; Follow-Up: From Week 24 up to Week 72

End point values	Follow-Up (FU) Period-nucleos(t)ide analog (NA)			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: percentage of subjects				
number (confidence interval 90%)	33.3 (14.17 to 57.74)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Requiring NA Re-treatment

End point title	Number of Subjects Requiring NA Re-treatment

End point description:

Number of subjects requiring NA re-treatment based on failure in NA treatment completion criteria (HBsAg <10 IU/mL, and HBeAg-negative, and HBV DNA < LLOQ (20 IU/m)L, and ALT <3*ULN) were reported. FAS included all subjects who were enrolled and who received at least 1 dose of study intervention within this ISA. Here "N" signifies the number of subjects that were evaluable for this endpoint and "n"(number of subjects analyzed) signifies number of subjects analyzed at specified timepoints. Data for this outcome measure was planned to be collected and analyzed for Follow-up Period only as pre-specified in protocol.

End point type	Secondary

End point timeframe:

Follow-up Period: From Week 24 up to Week 72

End point values	Follow-Up (FU) Period-nucleos(t)ide analog (NA)			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: subjects	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration 24 Hours after Administration (C24h) of JNJ-73763989 (JNJ-73763976 and JNJ-73763924)

End point title	Plasma Concentration 24 Hours after Administration (C24h) of JNJ-73763989 (JNJ-73763976 and JNJ-73763924)

End point description:

Plasma concentration 24 hours (C24h) after administration of JNJ-73763989 (JNJ-73763976 and JNJ-73763924) were reported. Pharmacokinetics(PK) Analysis Set included all subjects who received at least 1 dose of study intervention and had at least 1 valid blood sample drawn for PK analysis. Here "N" (Number of subjects that started the Arm) signifies the number of subjects that were evaluable for this

endpoint. Data for this endpoint was planned to be collected and analyzed for TP1 and TP2 only as specified in protocol.

End point type	Secondary

End point timeframe:

Treatment Period 1: Day 1 Week 1: Treatment Period 2: Day 1, Week 12

End point values	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: ng/mL				
arithmetic mean (standard deviation)				
JNJ-73763976	309 (± 145)	390 (± 162)		
JNJ-73763924	38.7 (± 16.2)	57.4 (± 15.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Observed Plasma Concentration (Tmax) of JNJ-73763989 (JNJ-73763976 and JNJ-73763924)

End point title	Time to Reach Maximum Observed Plasma Concentration (Tmax) of JNJ-73763989 (JNJ-73763976 and JNJ-73763924)

End point description:

Time to reach maximum observed plasma concentration (Cmax) (Tmax) of JNJ-73763989 (JNJ-73763976 and JNJ-73763924) were reported. Pharmacokinetics(PK) analysis set included all subjects who received at least 1 dose of study intervention and had at least 1 valid blood sample drawn for PK analysis. Here "N" (Number of subjects that started the Arm) signifies the number of subjects that were evaluable for this endpoint. Data for this endpoint was planned to be collected and analyzed for TP1 and TP2 only as specified in protocol.

End point type	Secondary

End point timeframe:

Treatment Period 1: Day 1, Week 1; Treatment Period 2: Day 1, Week 12

End point values	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: hours				
median (full range (min-max))				

JNJ-73763976 JNJ-73763924	5.50 (2.00 to 6.20) 2.00 (1.00 to 6.00)	6.00 (2.00 to 23.58) 4.02 (0.50 to 7.72)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration Versus Time Curve From Time 0 to 24 hour (AUC[0-24]h) of JNJ-73763989 (JNJ-73763976 and JNJ-73763924)

End point title	Area Under the Plasma Concentration Versus Time Curve From Time 0 to 24 hour (AUC[0-24]h) of JNJ-73763989 (JNJ-73763976 and JNJ-73763924)

End point description:

Area under the plasma concentration versus time curve from time 0 to 24 hour (AUC[0-24]h) of JNJ-73763989 (JNJ-73763976 and JNJ-73763924) were reported. Pharmacokinetics(PK) analysis set included all subjects who received at least 1 dose of study intervention and had at least 1 valid blood sample drawn for PK analysis. Here "N" (Number of subjects that started the Arm) signifies the number of subjects that were evaluable for this endpoint. Data for this endpoint was planned to be collected and analyzed for TP1 and TP2 only as specified in protocol.

End point type	Secondary

End point timeframe:

Treatment Period 1: Day 1, Week 1; Treatment Period 2: Day 1, Week 12

End point values	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: ng*h/mL				
arithmetic mean (standard deviation)				
JNJ-73763976 JNJ-73763924	18635 (± 10983) 3342 (± 1919)	13580 (± 8598) 2466 (± 1432)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment Period 1: From Baseline (Day 1) up to Week 12;
Treatment Period 2: From Week 12 up to Week 24;
Follow-Up: From Week 24 up to Week 72

Adverse event reporting additional description:

Safety analysis set included all participants who received at least 1 dose of study intervention. Participants were analyzed according to the study intervention they actually received.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA

Reporting group description:

Subjects received JNJ-73763989 (JNJ-3989) 200 milligrams (mg) as a subcutaneous injection (SC) every 4 weeks (Q4W) along with JNJ-56136379 (JNJ-6379) 250 mg tablet once daily (QD) and nucleos(t)ide analog (NA) treatment (either entecavir [ETV] 0.5 mg, tenofovir disoproxil fumarate [TDF] 245 mg, or tenofovir alafenamide [TAF] 25 mg) QD up to 12 weeks in TP 1. Subjects enrolled until Protocol Amendment 3, also received single dose of JNJ-6379 250 mg orally as part of their study intervention. Subjects enrolled after Protocol Amendment 3, received JNJ-3989 + PegIFN-alpha 2a + NA only. Subjects were assessed for eligibility criteria for PegIFN-alpha 2a at Week 12 and those who met the criteria entered TP 2.

Reporting group title	Follow-Up (FU) Period-nucleos(t)ide analog (NA)

Reporting group description:

At Week 24, prior to follow-up period, all subjects stopped treatment with JNJ-73763989 + JNJ-56136379 + PegIFN-alpha2a. Subjects who met the protocol-defined NA treatment completion criteria (hepatitis B surface antigen [HBsAg] <10 international units/millilitre [IU/mL], and hepatitis B e antigen [HBeAg]-negative, and hepatitis B virus deoxyribonucleic acid [HBV DNA] <lower limit of quantification [LLOQ], and alanine aminotransferase [ALT] <3*Upper limit of normal [ULN]) at Week 24, stopped NA at Week 26 (that is follow up Week 2). Subjects who did not meet NA completion criteria continued NA treatment during the follow-up period up to Week 72 (that is, follow-up Week 48).

Reporting group title	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA

Reporting group description:

Subjects who met the eligibility criteria for PegIFN-alpha2a (subjects who did not have disorders including but not limited to: autoimmune disorders, bone marrow suppression, hypoglycemia, hyperglycemia, diabetes mellitus) at Week 12 received combination treatment with JNJ-73763989 200 mg SC injection Q4W along with NA treatment (either ETV 0.5 mg, TDF 245 mg, or TAF 25 mg), QD up to Week 24 plus PegIFN-alpha 2a 180 micrograms (mcg) once weekly (Q1W) during TP 2. Subjects enrolled until Protocol Amendment 3, also received single dose of JNJ-6379 250 mg orally as part of their study intervention. Subjects enrolled after Protocol Amendment 3, received JNJ-3989 + PegIFN-alpha 2a + NA only.

Serious adverse events	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA	Follow-Up (FU) Period-nucleos(t)ide analog (NA)	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 48 (0.00%)	4 / 48 (8.33%)	1 / 48 (2.08%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gastric Cancer			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	0 / 48 (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
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic Mass			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	0 / 48 (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			
Hydronephrosis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	0 / 48 (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
Nephrolithiasis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	0 / 48 (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
Ureterolithiasis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	0 / 48 (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
Infections and infestations			
Urinary Tract Infection			

subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	0 / 48 (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

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

Non-serious adverse events	TP 1:JNJ-73763989 200 mg+JNJ-56136379 250 mg+NA	Follow-Up (FU) Period-nucleos(t)ide analog (NA)	TP 2:JNJ-3989 200 mg+JNJ-6379 250 mg+PegIFN-alpha2a 180 mcg+NA
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 48 (25.00%)	20 / 48 (41.67%)	35 / 48 (72.92%)
Investigations			
Neutrophil Count Decreased			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	4 / 48 (8.33%)
occurrences (all)	0	0	7
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	3 / 48 (6.25%)
occurrences (all)	2	0	4
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	3 / 48 (6.25%)
occurrences (all)	1	0	3
Headache			
subjects affected / exposed	3 / 48 (6.25%)	3 / 48 (6.25%)	4 / 48 (8.33%)
occurrences (all)	4	3	4
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 48 (6.25%)	1 / 48 (2.08%)	5 / 48 (10.42%)
occurrences (all)	3	1	5
Influenza Like Illness			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	6 / 48 (12.50%)
occurrences (all)	0	0	7
Pyrexia			
subjects affected / exposed	2 / 48 (4.17%)	2 / 48 (4.17%)	15 / 48 (31.25%)
occurrences (all)	2	2	18
Injection Site Erythema			

subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	7 / 48 (14.58%)
occurrences (all)	1	0	10
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	4 / 48 (8.33%)
occurrences (all)	0	1	5
Neutropenia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	4 / 48 (8.33%)
occurrences (all)	0	0	6
Leukopenia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	3 / 48 (6.25%)
occurrences (all)	0	0	4
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	3 / 48 (6.25%)
occurrences (all)	0	0	3
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	4 / 48 (8.33%)
occurrences (all)	0	0	4
Myalgia			
subjects affected / exposed	2 / 48 (4.17%)	0 / 48 (0.00%)	9 / 48 (18.75%)
occurrences (all)	2	0	9
Infections and infestations			
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 48 (2.08%)	3 / 48 (6.25%)	0 / 48 (0.00%)
occurrences (all)	1	7	0
Nasopharyngitis			
subjects affected / exposed	1 / 48 (2.08%)	3 / 48 (6.25%)	1 / 48 (2.08%)
occurrences (all)	1	3	1
Covid-19			
subjects affected / exposed	0 / 48 (0.00%)	13 / 48 (27.08%)	1 / 48 (2.08%)
occurrences (all)	0	13	1
Metabolism and nutrition disorders			
Decreased Appetite			

subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 48 (0.00%) 0	5 / 48 (10.42%) 5

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 December 2021	The purpose of this amendment was to update the criteria for post-treatment monitoring and for nucleos(t)ide analog (NA) re-treatment for subjects who discontinued NA treatment at follow-up Week 2.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported