Clinical trial results:
A Phase 2 Randomized, Open-label, Parallel-group, Multicenter Study to Assess Intrahepatic and PeripheralChanges of Immunologic and Virologic Markers in Response to Combination Regimens Containing JNJ-73763989 and Nucleos(t)ide Analog With or Without JNJ-56136379 in Patients With Chronic Hepatitis B Virus Infection

Summary

EudraCT number	2019-004475-39
Trial protocol	BE FR DE PL IT
Global end of trial date	01 September 2024

Results information

Result version number	v1 (current)
This version publication date	11 April 2025
First version publication date	11 April 2025

Trial information

Trial identification

Sponsor protocol code	73763989HPB2003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04585789
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development, a division of Janssen Pharmaceutica NV
Sponsor organisation address	Janssen Research & Development, a division of Janssen Pharmaceutica NV, Beerse, Belgium, 2340
Public contact	Clinical Registry Group, Janssen Research & Development, a division of Janssen Pharmaceutica NV, ClinicalTrialsEU@its.jnj.com
Scientific contact	ClinicalTrialsEU@its.jnj.com, Janssen Research & Development, a division of Janssen Pharmaceutica NV, 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	01 September 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 September 2024
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 changes in intrahepatic hepatitis B surface antigen (HBsAg) between baseline and on-treatment liver biopsy in Panels 1 and 2 and to assess changes in drug concentrations over time in Panel 3 during JNJ-73763989 (JNJ-3989) treatment-based combination treatment.

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	11 March 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	New Zealand: 3
Country: Number of subjects enrolled	Poland: 1
Country: Number of subjects enrolled	United States: 1
Worldwide total number of subjects	24
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)	24
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Nucleos(t)ide analog (NA) treatment completion criteria (alanine aminotransferase [ALT] less than [<]3*upper limit of normal[ULN], HB virus deoxyribonucleic acid [HBV DNA] <lower limit of quantification [LLOQ]:20 International Units per milliliter [IU/mL], HBeAg negative & HB surface antigen [HBsAg] <10 IU/mL).

Pre-assignment

Screening details:

Per protocol amendment (PA) 5 (01 October 2021), all subjects stopped JNJ-56136379 (JNJ-6379) treatment and continued treatment with JNJ-73763989 (JNJ-3989) plus nucleos(t)ide analog (NA; ETV, TD, or TAF) plus optional pegylated interferon alpha-2a (PegIFN-alpha2a). Study consisted of 3 phases: screening phase, OL intervention phase and FU phase.

Period 1

Period 1 title	Open Label(OL) Phase: Week 1 to Week 48
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	OL Phase: Panel 1

Arm description:

Prior to PA 5, subjects received either JNJ-3989 200 milligrams (mg) subcutaneous(SC) injection every 4 weeks(Q4W) from Day 1 (Week 1) to Week 44+JNJ-6379 250 mg once daily(QD)+NA (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48 or JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1) to Week 44+NA (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48. After PA 5, subjects stopped JNJ-6379 and continued JNJ-3989+NA. With separate consent, subjects received optional treatment: PegIFN-alpha-2a 180 micrograms(mcg) SC injection once weekly(QW) post Week 40 liver biopsy for either 12 or 24 weeks (anytime between study Week 40 to 72) at investigator's discretion. At end of treatment Week 48, all subjects entered FU phase and stopped JNJ-3989/JNJ-6379 and NA (if NA treatment completion criteria was met as per Week 44 laboratory tests). If NA treatment completion criteria were not met at Week 48, NA was continued till FU phase end (study Week 96).

Arm type	Experimental
Investigational medicinal product name	JNJ-73763989
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received JNJ-73763989 200 mg SC injection once every 4 weeks from Day 1 up to Week 44.

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

Dosage and administration details:

Subjects received JNJ-56136379 250 mg SC injection QD from Day 1 up to Week 48.

Investigational medicinal product name	Entecavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details: Subjects received entecavir 0.5 mg tablet QD from Day 1 up to Week 48.	
Investigational medicinal product name	Tenofovir Disoproxil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Subjects received tenofovir disoproxil 245 mg tablet QD from Day 1 up to Week 48.	
Investigational medicinal product name	Tenofovir Alafenamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Subjects received tenofovir alafenamide 25 mg tablet QD from Day 1 up to Week 48.	
Investigational medicinal product name	PegIFN-alpha-2a
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details: Subjects received PegIFN-alpha-2a 180 mcg SC injection QW for either 12 or 24 weeks.	
Arm title	OL Phase: Panel 2
Arm description: Prior to PA 5, subjects received either JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1) to Week 44 + JNJ-6379 250 mg QD and NA treatment (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48, or JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1) to Week 44 + NA (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48. After PA 5, subjects discontinued JNJ-6379 and continued JNJ-3989 + NA. With separate consent, subjects received optional treatment with PegIFNalpha-2a 180 mcg SC injection QW after Week 40 liver biopsy for either 12 or 24 weeks (anytime between study Week 40 to 72) at investigator's discretion. At end of treatment Week 48, all subjects entered FU phase and stopped JNJ-3989/JNJ-6379 and NA (if NA treatment completion criteria was met as per Week 44 laboratory tests). If NA treatment completion criteria were not met at Week 48, NA was continued till FU phase end (study Week 96).	
Arm type	Experimental
Investigational medicinal product name	JNJ-73763989
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details: Subjects received JNJ-73763989 200 mg SC injection once every 4 weeks from Day 1 up to Week 44.	
Investigational medicinal product name	JNJ-56136379
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Subjects received JNJ-56136379 250 mg SC injection QD from Day 1 up to Week 48.	
Investigational medicinal product name	Entecavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet

Routes of administration	Oral use
Dosage and administration details: Subjects received entecavir 0.5 mg tablet QD from Day 1 up to Week 48.	
Investigational medicinal product name	Tenofovir Disoproxil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Subjects received tenofovir disoproxil 245 mg tablet QD from Day 1 up to Week 48.	
Investigational medicinal product name	Tenofovir Alafenamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Subjects received tenofovir alafenamide 25 mg tablet QD from Day 1 up to Week 48.	
Investigational medicinal product name	PegIFN-alpha-2a
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details: Subjects received PegIFN-alpha-2a 180 mcg SC injection QW for either 12 or 24 weeks.	
Arm title	OL Phase: Panel 3

Arm description:

After PA 5, subjects received either JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1 to Week 44) + JNJ-6379 250 mg QD and NA treatment (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48, or JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1) to Week 44 + NA (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48. After PA 5, subjects discontinued JNJ-6379 and continued JNJ-3989 + NA. With separate consent, subjects received optional treatment with PegIFNalpha-2a 180 mcg SC injection QW after Week 40 liver biopsy for either 12 or 24 weeks (anytime between study Week 40 to 72) at investigator's discretion. At end of treatment Week 48, all subjects entered FU phase and stopped JNJ-3989/JNJ-6379 and NA (if NA treatment completion criteria was met as per Week 44 laboratory tests). If NA treatment completion criteria were not met at Week 48, NA was continued till FU phase end (study Week 96).

Arm type	Experimental
Investigational medicinal product name	JNJ-73763989
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details: Subjects received JNJ-73763989 200 mg SC injection once every 4 weeks from Day 1 up to Week 44.	
Investigational medicinal product name	Entecavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Subjects received entecavir 0.5 mg tablet QD from Day 1 up to Week 48.	
Investigational medicinal product name	PegIFN-alpha-2a
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received PegIFN-alpha-2a 180 mcg SC injection QW for either 12 or 24 weeks.

Investigational medicinal product name	Tenofovir Alafenamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received tenofovir alafenamide 25 mg tablet QD from Day 1 up to Week 48.

Investigational medicinal product name	Tenofovir Disoproxil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received tenofovir disoproxil 245 mg tablet QD from Day 1 up to Week 48.

Number of subjects in period 1	OL Phase: Panel 1	OL Phase: Panel 2	OL Phase: Panel 3
Started	10	10	4
Completed	10	10	4

Period 2

Period 2 title	Follow-up (FU) Phase: Week 48 to 96
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Follow-up Phase: Panel 1

Arm description:

After completion of open-label phase (up to 48 weeks) all subjects (with HBeAg positive and not currently treated) enrolled prior to PA 5, entered FU phase & stopped all study drugs including NA treatment, but NA treatment continued till end of FU (study Week 96), if NA treatment completion criteria (ALT: <3*ULN, HBV DNA <LLOQ:20 IU/mL, HBeAg negative and HBsAg<10 IU/mL) was not met at Week 48. Subjects on treatment with optional PegIFN-alpha-2a 180 mcg SC injection QW after Week 40 liver biopsy but had not met NA treatment completion criteria at Week 48, were assessed at end of treatment with PegIFN-α2a (study Week 60 or 72) and stopped NA, if NA treatment completion criteria were met. Subjects who met NA treatment completion criteria (at Week 48) were monitored Q4W in FU phase. If NA-retreatment criteria:HBV DNA >20,000 IU/mL, HBV DNA >2,000 IU/mL but <20,000 IU/mL & ALT>5*ULN was met, NA retreatment was started.

Arm type	Experimental

Investigational medicinal product name	Entecavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received entecavir 0.5 mg tablet QD from Day 1 up to Week 48.

Investigational medicinal product name	Tenofovir Alafenamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received tenofovir alafenamide 25 mg tablet QD from Day 1 up to Week 48.

Investigational medicinal product name	Tenofovir Disoproxil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received tenofovir disoproxil 245 mg tablet QD from Day 1 up to Week 48.

Arm title	Follow-up Phase: Panel 2

Arm description:

After completion of open-label phase (up to 48 weeks) all subjects (with HBeAg negative & virologically suppressed by ETV, TD, or TAF treatment) enrolled prior to PA 5, entered FU phase & stopped all study drugs including NA treatment, but NA treatment continued till end of FU (study Week 96), if NA treatment completion criteria (ALT: <3*ULN, HBV DNA <LLOQ:20 IU/mL, HBeAg negative and HBsAg<10 IU/mL) was not met at Week 48. Subjects who were on treatment with optional PegIFN-alpha-2a 180 mcg SC injection QW after Week 40 liver biopsy but had not met NA treatment completion criteria at Week 48, were assessed at the end of treatment with PegIFN-α2a (study Week 60 or 72) and stopped NA, if the NA treatment completion criteria were met. Subjects who met NA treatment completion criteria (at Week48) were monitored Q4W in FU phase. If NA-retreatment criteria (HBV DNA >20,000 IU/mL, HBV DNA >2,000 IU/mL but <20,000 IU/mL & ALT >5*ULN) was met, NA retreatment was started.

Arm type	Experimental
Investigational medicinal product name	Entecavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received entecavir 0.5 mg tablet QD from Day 1 up to Week 48.

Investigational medicinal product name	Tenofovir Alafenamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received tenofovir alafenamide 25 mg tablet QD from Day 1 up to Week 48.

Investigational medicinal product name	Tenofovir Disoproxil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received tenofovir disoproxil 245 mg tablet QD from Day 1 up to Week 48.

Arm title	Follow-up Phase: Panel 3

Arm description:

After completion of open-label phase (up to 48 weeks) subjects (HBeAg positive or negative & were either not currently treated or virologically suppressed by ETV or TD treatment) enrolled after PA 5, entered FU phase & stopped all study drugs including NA, but NA treatment continued till end of FU (study Week 96), if NA treatment completion criteria ([ALT <3*ULN, HBV DNA <LLOQ; 20 IU/mL, HBeAg negative and HBsAg <10 IU/mL]) was not met at Week 48. Subjects on treatment with optional PegIFNalpha-2a 180 mcg SC injection QW post Week 40 liver biopsy but had not met NA treatment completion criteria at Week 48, were assessed at end of treatment with PegIFN-α2a (study Week 60 or 72) & stopped NA, if NA treatment completion criteria were met. Subjects who met NA treatment completion criteria (at Week 48) were monitored Q4W in FU phase. If NA-retreatment criteria (HBV DNA >20,000 IU/mL, HBV DNA >2,000 IU/mL but <20,000 IU/mL & ALT >5*ULN) was met, NA retreatment was started.

Arm type	Experimental
Investigational medicinal product name	Entecavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received entecavir 0.5 mg tablet QD from Day 1 up to Week 48.

Investigational medicinal product name	Tenofovir Disoproxil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received tenofovir disoproxil 245 mg tablet QD from Day 1 up to Week 48.

Investigational medicinal product name	Tenofovir Alafenamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received tenofovir alafenamide 25 mg tablet QD from Day 1 up to Week 48.

Number of subjects in period 2	Follow-up Phase: Panel 1	Follow-up Phase: Panel 2	Follow-up Phase: Panel 3
Started	10	10	4
Completed	8	10	4
Not completed	2	0	0
Consent withdrawn by subject	1	-	-
Lost to follow-up	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	OL Phase: Panel 1

Reporting group description:

Prior to PA 5, subjects received either JNJ-3989 200 milligrams (mg) subcutaneous(SC) injection every 4 weeks(Q4W) from Day 1 (Week 1) to Week 44+JNJ-6379 250 mg once daily(QD)+NA (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48 or JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1) to Week 44+NA (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48. After PA 5, subjects stopped JNJ-6379 and continued JNJ-3989+NA. With separate consent, subjects received optional treatment: PegIFN-alpha-2a 180 micrograms(mcg) SC injection once weekly(QW) post Week 40 liver biopsy for either 12 or 24 weeks (anytime between study Week 40 to 72) at investigator's discretion. At end of treatment Week 48, all subjects entered FU phase and stopped JNJ-3989/JNJ-6379 and NA (if NA treatment completion criteria was met as per Week 44 laboratory tests). If NA treatment completion criteria were not met at Week 48, NA was continued till FU phase end (study Week 96).

Reporting group title	OL Phase: Panel 2

Reporting group description:

Prior to PA 5, subjects received either JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1) to Week 44 + JNJ-6379 250 mg QD and NA treatment (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48, or JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1) to Week 44 + NA (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48. After PA 5, subjects discontinued JNJ-6379 and continued JNJ-3989 + NA. With separate consent, subjects received optional treatment with PegIFNalpha-2a 180 mcg SC injection QW after Week 40 liver biopsy for either 12 or 24 weeks (anytime between study Week 40 to 72) at investigator's discretion. At end of treatment Week 48, all subjects entered FU phase and stopped JNJ-3989/JNJ-6379 and NA (if NA treatment completion criteria was met as per Week 44 laboratory tests). If NA treatment completion criteria were not met at Week 48, NA was continued till FU phase end (study Week 96).

Reporting group title	OL Phase: Panel 3

Reporting group description:

After PA 5, subjects received either JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1 to Week 44) + JNJ-6379 250 mg QD and NA treatment (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48, or JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1) to Week 44 + NA (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48. After PA 5, subjects discontinued JNJ-6379 and continued JNJ-3989 + NA. With separate consent, subjects received optional treatment with PegIFNalpha-2a 180 mcg SC injection QW after Week 40 liver biopsy for either 12 or 24 weeks (anytime between study Week 40 to 72) at investigator's discretion. At end of treatment Week 48, all subjects entered FU phase and stopped JNJ-3989/JNJ-6379 and NA (if NA treatment completion criteria was met as per Week 44 laboratory tests). If NA treatment completion criteria were not met at Week 48, NA was continued till FU phase end (study Week 96).

Reporting group values	OL Phase: Panel 1	OL Phase: Panel 2	OL Phase: Panel 3
Number of subjects	10	10	4
Age Categorical Units: Subjects			
Age continuous Units: Years arithmetic mean standard deviation	 33.4 ± 14.73	 43.4 ± 12.63	 42 ± 12.73
Gender categorical Units: Subjects			
Male	5	5	4
Female	5	5	0
Age Categorical Units: Subjects			
Children (2-11 years)	0	0	0

Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	10	10	4
From 65 to 84 years	0	0	0
85 years and over	0	0	0

Reporting group values	Total		
Number of subjects	24		
Age Categorical Units: Subjects			

Age continuous Units: Years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Male	14		
Female	10		
Age Categorical Units: Subjects			
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	24		
From 65 to 84 years	0		
85 years and over	0		

Subject analysis sets

Subject analysis set title	Panel 1
Subject analysis set type	Per protocol

Subject analysis set description:

Prior to PA 5, subjects received either JNJ-3989 200 milligrams (mg) subcutaneous(SC) injection every 4 weeks(Q4W) from Day 1 (Week 1) to Week 44+JNJ-6379 250 mg once daily(QD)+NA (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48 or JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1) to Week 44+NA (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48. After PA 5, subjects stopped JNJ-6379 and continued JNJ-3989+NA. With separate consent, subjects received optional treatment: PegIFN-alpha-2a 180 micrograms(mcg) SC injection once weekly(QW) post Week 40 liver biopsy for either 12 or 24 weeks (anytime between study Week 40 to 72) at investigator's discretion. At end of treatment Week 48, all subjects entered FU phase and stopped JNJ-3989/JNJ-6379 and NA, if NA treatment completion criteria was met as per Week 44 laboratory tests. If NA treatment completion criteria were not met at Week 48, NA was continued till FU phase end (study Week 96).

Subject analysis set title	Panel 2
Subject analysis set type	Per protocol

Subject analysis set description:

Prior to PA 5, subjects received either JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1) to Week 44 + JNJ-6379 250 mg QD and NA treatment (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48, or JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1) to Week 44 + NA (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48. After PA 5, subjects discontinued JNJ-6379 and continued JNJ-3989 + NA. With separate consent, subjects received optional treatment with PegIFNalpha-2a 180 mcg SC injection QW after Week 40 liver biopsy for either 12 or 24 weeks (anytime between study Week 40 to 72) at investigator's discretion. At end of treatment Week 48, all subjects entered FU phase and stopped JNJ-3989/JNJ-6379 and NA (if NA treatment completion criteria was met as per Week 44 laboratory tests). If NA treatment completion criteria were not met at Week 48, NA was continued till FU phase end (study Week 96).

Subject analysis set title	Panel 3
Subject analysis set type	Per protocol

Subject analysis set description:

After PA 5, subjects received either JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1 to Week 44) + JNJ-6379 250 mg QD and NA treatment (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48, or JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1) to Week 44 + NA (ETV 0.5 mg/ TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48. After PA 5, subjects discontinued JNJ-6379 and continued JNJ-3989 + NA. With separate consent, subjects received optional treatment with PegIFNalpha- 2a 180 mcg SC injection QW after Week 40 liver biopsy for either 12 or 24 weeks (anytime between study Week 40 to 72) at investigator's discretion. At end of treatment Week 48, all subjects entered FU phase and stopped JNJ-3989/JNJ-6379 and NA (if NA treatment completion criteria was met as per Week 44 laboratory tests). If NA treatment completion criteria were not met at Week 48, NA was continued till FU phase end (study Week 96).

Reporting group values	Panel 1	Panel 2	Panel 3
Number of subjects	10	10	4
Age Categorical Units: Subjects			
Age continuous Units: Years			
arithmetic mean	0	0	0
standard deviation	±	±	±
Gender categorical Units: Subjects			
Male	0	0	0
Female	0	0	0
Age Categorical Units: Subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65 to 84 years	0	0	0
85 years and over	0	0	0

End points reporting groups

Reporting group title	OL Phase: Panel 1

Reporting group description:

Prior to PA 5, subjects received either JNJ-3989 200 milligrams (mg) subcutaneous(SC) injection every 4 weeks(Q4W) from Day 1 (Week 1) to Week 44+JNJ-6379 250 mg once daily(QD)+NA (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48 or JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1) to Week 44+NA (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48. After PA 5, subjects stopped JNJ-6379 and continued JNJ-3989+NA. With separate consent, subjects received optional treatment: PegIFN-alpha-2a 180 micrograms(mcg) SC injection once weekly(QW) post Week 40 liver biopsy for either 12 or 24 weeks (anytime between study Week 40 to 72) at investigator's discretion. At end of treatment Week 48, all subjects entered FU phase and stopped JNJ-3989/JNJ-6379 and NA (if NA treatment completion criteria was met as per Week 44 laboratory tests). If NA treatment completion criteria were not met at Week 48, NA was continued till FU phase end (study Week 96).

Reporting group title	OL Phase: Panel 2

Reporting group description:

Prior to PA 5, subjects received either JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1) to Week 44 + JNJ-6379 250 mg QD and NA treatment (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48, or JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1) to Week 44 + NA (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48. After PA 5, subjects discontinued JNJ-6379 and continued JNJ-3989 + NA. With separate consent, subjects received optional treatment with PegIFNalpha-2a 180 mcg SC injection QW after Week 40 liver biopsy for either 12 or 24 weeks (anytime between study Week 40 to 72) at investigator's discretion. At end of treatment Week 48, all subjects entered FU phase and stopped JNJ-3989/JNJ-6379 and NA (if NA treatment completion criteria was met as per Week 44 laboratory tests). If NA treatment completion criteria were not met at Week 48, NA was continued till FU phase end (study Week 96).

Reporting group title	OL Phase: Panel 3

Reporting group description:

After PA 5, subjects received either JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1 to Week 44) + JNJ-6379 250 mg QD and NA treatment (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48, or JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1) to Week 44 + NA (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48. After PA 5, subjects discontinued JNJ-6379 and continued JNJ-3989 + NA. With separate consent, subjects received optional treatment with PegIFNalpha-2a 180 mcg SC injection QW after Week 40 liver biopsy for either 12 or 24 weeks (anytime between study Week 40 to 72) at investigator's discretion. At end of treatment Week 48, all subjects entered FU phase and stopped JNJ-3989/JNJ-6379 and NA (if NA treatment completion criteria was met as per Week 44 laboratory tests). If NA treatment completion criteria were not met at Week 48, NA was continued till FU phase end (study Week 96).

Reporting group title	Follow-up Phase: Panel 1

Reporting group description:

After completion of open-label phase (up to 48 weeks) all subjects (with HBeAg positive and not currently treated) enrolled prior to PA 5, entered FU phase & stopped all study drugs including NA treatment, but NA treatment continued till end of FU (study Week 96), if NA treatment completion criteria (ALT: <3*ULN, HBV DNA <LLOQ:20 IU/mL, HBeAg negative and HBsAg<10 IU/mL) was not met at Week 48. Subjects on treatment with optional PegIFN-alpha-2a 180 mcg SC injection QW after Week 40 liver biopsy but had not met NA treatment completion criteria at Week 48, were assessed at end of treatment with PegIFN-α2a (study Week 60 or 72) and stopped NA, if NA treatment completion criteria were met. Subjects who met NA treatment completion criteria (at Week 48) were monitored Q4W in FU phase. If NA-retreatment criteria:HBV DNA >20,000 IU/mL, HBV DNA >2,000 IU/mL but <20,000 IU/mL & ALT>5*ULN was met, NA retreatment was started.

Reporting group title	Follow-up Phase: Panel 2

Reporting group description:

After completion of open-label phase (up to 48 weeks) all subjects (with HBeAg negative & virologically suppressed by ETV, TD, or TAF treatment) enrolled prior to PA 5, entered FU phase & stopped all study drugs including NA treatment, but NA treatment continued till end of FU (study Week 96), if NA treatment completion criteria (ALT: <3*ULN, HBV DNA <LLOQ:20 IU/mL, HBeAg negative and HBsAg<10 IU/mL) was not met at Week 48. Subjects who were on treatment with optional PegIFN-alpha-2a 180 mcg SC injection QW after Week 40 liver biopsy but had not met NA treatment completion criteria at Week 48, were assessed at the end of treatment with PegIFN-α2a (study Week 60 or 72) and stopped NA, if the NA treatment completion criteria were met. Subjects who met NA treatment completion criteria (at Week48) were monitored Q4W in FU phase. If NA-retreatment criteria (HBV DNA >20,000 IU/mL, HBV DNA >2,000 IU/mL but <20,000 IU/mL & ALT >5*ULN) was met, NA retreatment

was started.

Reporting group title	Follow-up Phase: Panel 3

Reporting group description:

After completion of open-label phase (up to 48 weeks) subjects (HBeAg positive or negative & were either not currently treated or virologically suppressed by ETV or TD treatment) enrolled after PA 5, entered FU phase & stopped all study drugs including NA, but NA treatment continued till end of FU (study Week 96), if NA treatment completion criteria ([ALT <3*ULN, HBV DNA <LLOQ; 20 IU/mL, HBeAg negative and HBsAg <10 IU/mL]) was not met at Week 48. Subjects on treatment with optional PegIFNalpha-2a 180 mcg SC injection QW post Week 40 liver biopsy but had not met NA treatment completion criteria at Week 48, were assessed at end of treatment with PegIFN-α2a (study Week 60 or 72) & stopped NA, if NA treatment completion criteria were met. Subjects who met NA treatment completion criteria (at Week 48) were monitored Q4W in FU phase. If NA-retreatment criteria (HBV DNA >20,000 IU/mL, HBV DNA >2,000 IU/mL but <20,000 IU/mL & ALT >5*ULN) was met, NA retreatment was started.

Subject analysis set title	Panel 1
Subject analysis set type	Per protocol

Subject analysis set description:

Prior to PA 5, subjects received either JNJ-3989 200 milligrams (mg) subcutaneous(SC) injection every 4 weeks(Q4W) from Day 1 (Week 1) to Week 44+JNJ-6379 250 mg once daily(QD)+NA (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48 or JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1) to Week 44+NA (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48. After PA 5, subjects stopped JNJ-6379 and continued JNJ-3989+NA. With separate consent, subjects received optional treatment: PegIFN-alpha-2a 180 micrograms(mcg) SC injection once weekly(QW) post Week 40 liver biopsy for either 12 or 24 weeks (anytime between study Week 40 to 72) at investigator's discretion. At end of treatment Week 48, all subjects entered FU phase and stopped JNJ-3989/JNJ-6379 and NA, if NA treatment completion criteria was met as per Week 44 laboratory tests. If NA treatment completion criteria were not met at Week 48, NA was continued till FU phase end (study Week 96).

Subject analysis set title	Panel 2
Subject analysis set type	Per protocol

Subject analysis set description:

Prior to PA 5, subjects received either JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1) to Week 44 + JNJ-6379 250 mg QD and NA treatment (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48, or JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1) to Week 44 + NA (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48. After PA 5, subjects discontinued JNJ-6379 and continued JNJ-3989 + NA. With separate consent, subjects received optional treatment with PegIFNalpha-2a 180 mcg SC injection QW after Week 40 liver biopsy for either 12 or 24 weeks (anytime between study Week 40 to 72) at investigator's discretion. At end of treatment Week 48, all subjects entered FU phase and stopped JNJ-3989/JNJ-6379 and NA (if NA treatment completion criteria was met as per Week 44 laboratory tests). If NA treatment completion criteria were not met at Week 48, NA was continued till FU phase end (study Week 96).

Subject analysis set title	Panel 3
Subject analysis set type	Per protocol

Subject analysis set description:

After PA 5, subjects received either JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1 to Week 44) + JNJ-6379 250 mg QD and NA treatment (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48, or JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1) to Week 44 + NA (ETV 0.5 mg/ TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48. After PA 5, subjects discontinued JNJ-6379 and continued JNJ-3989 + NA. With separate consent, subjects received optional treatment with PegIFNalpha- 2a 180 mcg SC injection QW after Week 40 liver biopsy for either 12 or 24 weeks (anytime between study Week 40 to 72) at investigator's discretion. At end of treatment Week 48, all subjects entered FU phase and stopped JNJ-3989/JNJ-6379 and NA (if NA treatment completion criteria was met as per Week 44 laboratory tests). If NA treatment completion criteria were not met at Week 48, NA was continued till FU phase end (study Week 96).

Primary: Panel 1 and 2: Absolute Change From Baseline in the Percentage of Hepatitis B Surface Antigen (HBsAg) Hepatocytes at Week 40

End point title	Panel 1 and 2: Absolute Change From Baseline in the Percentage of Hepatitis B Surface Antigen (HBsAg) Hepatocytes at Week 40[1][2]

End point description:

Absolute change from baseline to on-treatment liver biopsy timepoint (Week 40) in terms of the percentage of HBsAg-positive hepatocytes (at Week 40) were reported. Intent-to-treat (ITT) population included subjects who were randomly assigned or enrolled to an intervention arm and received at least

1 dose of intervention. Subjects were analyzed according to study intervention they were randomly assigned or enrolled. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint. Data for this endpoint was planned to be collected and analyzed for Panels 1 and 2 alone.

End point type	Primary

End point timeframe:

Baseline, Week 40

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 inferential statistics was done. Only descriptive statistics was performed.

[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: Data for this endpoint was planned to be collected and analyzed for Panels 1 and 2 alone.

End point values	OL Phase: Panel 1	OL Phase: Panel 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	9		
Units: percentage of HBsAg hepatocytes				
arithmetic mean (confidence interval 80%)	-78.46 (-94.078 to -42.936)	-5.68 (-15.846 to -0.885)		

Statistical analyses

No statistical analyses for this end point

Primary: Panel 3: Liver Concentrations of JNJ-73763989 (JNJ-73763976, JNJ-73763924 and M65; Deaminated Metabolite of JNJ-73763976) at Week 12

End point title	Panel 3: Liver Concentrations of JNJ-73763989 (JNJ-73763976, JNJ-73763924 and M65; Deaminated Metabolite of JNJ-73763976) at Week 12[3][4]

End point description:

Liver concentrations of JNJ-73763989 (JNJ-73763976, JNJ-73763924 and M65; Deaminated Metabolite of JNJ-73763976) at Week 12 were reported. ITT population included subjects who were randomly assigned or enrolled to an intervention arm and received at least 1 dose of intervention. Subjects were analyzed according to study intervention they were randomly assigned or enrolled. Data for this endpoint was planned to be collected and analyzed for Panel 3 alone.

End point type	Primary

End point timeframe:

At Week 12 (at the time of liver biopsy: 24 hours post dose of JNJ-73763989)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistics was done. Only descriptive statistics was performed.

[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: Data for this endpoint was planned to be collected and analyzed for Panel 3 alone.

End point values	OL Phase: Panel 3			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: ng/g				
arithmetic mean (standard deviation)				
JNJ-73763976	3550.00 (± 1674.714)			
JNJ-73763924	87300.00 (± 31712.668)			
M65	66175.00 (± 26000.817)			

Statistical analyses

No statistical analyses for this end point

Primary: Panel 3: Liver Concentrations of JNJ-73763989 (JNJ-73763976, JNJ-73763924 and M65; Deaminated Metabolite of JNJ-73763976) at Week 40

End point title	Panel 3: Liver Concentrations of JNJ-73763989 (JNJ-73763976, JNJ-73763924 and M65; Deaminated Metabolite of JNJ-73763976) at Week 40[5][6]

End point description:

Liver concentrations of JNJ-73763989 (JNJ-73763976, JNJ-73763924 molecules of JNJ-73763989) and JNJ-87719164 (M65: determined metabolite of JNJ-73763976) at Week 40 were reported. ITT population included subjects who were randomly assigned or enrolled to an intervention arm and received at least 1 dose of intervention. Subjects were analyzed according to study intervention they were randomly assigned or enrolled. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint. Data for this endpoint was planned to be collected and analyzed for Panel 3 alone.

End point type	Primary

End point timeframe:

At Week 40 (at the time of liver biopsy: 24 hours post dose of JNJ-73763989)

Notes:

[5] - 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 inferential statistics was done. Only descriptive statistics was performed.

[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: Data for this endpoint was planned to be collected and analyzed for Panel 3 alone.

End point values	OL Phase: Panel 3			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: ng/g				
arithmetic mean (standard deviation)				
JNJ-73763976	5883.33 (± 2147.145)			
JNJ-73763924	208666.67 (± 66860.551)			
M65	133800.00 (± 50615.413)			

Statistical analyses

No statistical analyses for this end point

Primary: Panel 3: Plasma Concentration of JNJ-73763989 (JNJ-73763976, JNJ-73763924 and M65; Deaminated Metabolite of JNJ-73763976) at Week 12

End point title	Panel 3: Plasma Concentration of JNJ-73763989 (JNJ-73763976, JNJ-73763924 and M65; Deaminated Metabolite of JNJ-73763976) at Week 12[7][8]

End point description:

Plasma concentration of JNJ-73763989 (JNJ-73763976, JNJ-73763924 and M65; Deaminated Metabolite of JNJ-73763976) at Week 12 were reported. ITT population included subjects who were randomly assigned or enrolled to an intervention arm and received at least 1 dose of intervention. Subjects were analyzed according to study intervention they were randomly assigned or enrolled. Data for this endpoint was planned to be collected and analyzed for Panel 3 alone.

End point type	Primary

End point timeframe:

At Week 12 (at the time of liver biopsy: 24 hours post dose of JNJ-73763989)

Notes:

[7] - 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 inferential statistics was done. Only descriptive statistics was performed.

[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: Data for this endpoint was planned to be collected and analyzed for Panel 3 alone.

End point values	OL Phase: Panel 3			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
JNJ-73763976	254.70 (± 123.841)			
JNJ-73763924	36.18 (± 22.667)			

Statistical analyses

No statistical analyses for this end point

Primary: Panel 3: Plasma Concentrations of JNJ-73763989 (JNJ-73763976 and JNJ-73763924) at Week 40

End point title	Panel 3: Plasma Concentrations of JNJ-73763989 (JNJ-73763976 and JNJ-73763924) at Week 40[9][10]

End point description:

Plasma concentrations of JNJ-73763989 (JNJ-73763976 and JNJ-73763924 molecules of JNJ-73763989)

at Week 40 were reported. ITT population included subjects who were randomly assigned or enrolled to an intervention arm and received at least 1 dose of intervention. Subjects were analyzed according to study intervention they were randomly assigned or enrolled. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint. Data for this endpoint was planned to be collected and analyzed for Panel 3 alone.

End point type	Primary

End point timeframe:

At Week 40 (at the time of liver biopsy: 24 hours post dose of JNJ-73763989)

Notes:

[9] - 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 inferential statistics was done. Only descriptive statistics was performed.

[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: Data for this endpoint was planned to be collected and analyzed for Panel 3 alone.

End point values	OL Phase: Panel 3			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: ng/mL				
arithmetic mean (standard deviation)				
JNJ-73763976	530.97 (± 176.408)			
JNJ-73763924	74.87 (± 12.788)			

Statistical analyses

No statistical analyses for this end point

Primary: Panel 3: Correlation of Liver Concentration to Plasma Concentration of JNJ-73763989 (JNJ-73763976 and JNJ-73763924) and Liver Concentration of M65 (Deaminated Metabolite of JNJ-73763976) to Liver Concentration JNJ-73763976 at Week 12

End point title	Panel 3: Correlation of Liver Concentration to Plasma Concentration of JNJ-73763989 (JNJ-73763976 and JNJ-73763924) and Liver Concentration of M65 (Deaminated Metabolite of JNJ-73763976) to Liver Concentration JNJ-73763976 at Week 12[11][12]

End point description:

Correlation of liver concentration to plasma concentration of JNJ-73763989 (JNJ-73763976 and liver concentration of M65 (Deaminated metabolite of JNJ-73763976) to liver concentration JNJ-73763976 at Week 12 were reported. ITT population included subjects who were randomly assigned or enrolled to an intervention arm and received at least 1 dose of intervention. Subjects were analyzed according to study intervention they were randomly assigned or enrolled. Data for this endpoint was planned to be collected and analyzed for Panel 3 alone.

End point type	Primary

End point timeframe:

Week 12 (at the time of liver biopsy: 24 hours post dose of JNJ-73763989)

Notes:

[11] - 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 inferential statistics was done. Only descriptive statistics was performed.

[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: Data for this endpoint was planned to be collected and analyzed for Panel 3 alone.

End point values	OL Phase: Panel 3			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: ratio				
arithmetic mean (standard deviation)				
JNJ-73763976 (liver to plasma concentration)	14.51 (± 4.725)			
JNJ-73763924 (liver to plasma concentration)	2844.26 (± 1265.202)			
M65 to JNJ-73763976(liver to liver concentration)	19.47 (± 3.267)			

Statistical analyses

No statistical analyses for this end point

Primary: Panel 3: Correlation of Liver to Plasma Concentration of JNJ-73763989 (JNJ-73763976 and JNJ-73763924) and Liver Concentration of M65 (Deaminated Metabolite of JNJ-73763976) to Liver Concentration JNJ-73763976 at Week 40

End point title	Panel 3: Correlation of Liver to Plasma Concentration of JNJ-73763989 (JNJ-73763976 and JNJ-73763924) and Liver Concentration of M65 (Deaminated Metabolite of JNJ-73763976) to Liver Concentration JNJ-73763976 at Week 40[13][14]

End point description:

Correlation of liver concentration to plasma concentration of JNJ-73763989 (JNJ-73763976 and liver concentration of M65 (Deaminated metabolite of JNJ-73763976) to liver concentration JNJ-73763976 at Week 40 were reported. ITT population included subjects who were randomly assigned or enrolled to an intervention arm and received at least 1 dose of intervention. Subjects were analyzed according to study intervention they were randomly assigned or enrolled. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint. Data for this endpoint was planned to be collected and analyzed for Panel 3 alone.

End point type	Primary

End point timeframe:

Week 40 (at the time of liver biopsy: 24 hours post dose of JNJ-73763989)

Notes:

[13] - 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 inferential statistics was done. Only descriptive statistics was performed.

[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: Data for this endpoint was planned to be collected and analyzed for Panel 3 alone.

End point values	OL Phase: Panel 3			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: ratio				
arithmetic mean (standard deviation)				
JNJ-73763976	12.67 (± 7.269)			
JNJ-73763924	2847.66 (± 1034.033)			
M65 to JNJ-73763976 liver concentration	22.65 (± 1.407)			

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 1 and 2: Change From Baseline in Percentage of Intrahepatic Viral Parameter: Hepatitis B Core Antigen Positive (HBcAg+) Hepatocytes at Week 40

End point title	Panel 1 and 2: Change From Baseline in Percentage of Intrahepatic Viral Parameter: Hepatitis B Core Antigen Positive (HBcAg+) Hepatocytes at Week 40

End point description:

Change from baseline in percentage of intrahepatic viral parameters HBcAg positive hepatocytes at Week 40 were reported. The percentage of HBcAg positive hepatocytes were derived as number of HBcAg positive hepatocytes*100 per total number of evaluated hepatocytes. ITT population included subjects who were randomly assigned or enrolled to an intervention arm and received at least 1 dose of intervention. Subjects were analyzed according to study intervention they were randomly assigned or enrolled. Here "N" (Number of subjects analyzed) signifies the number of subjects that were evaluable for this endpoint. Data for this endpoint was not planned to be collected and analyzed for Panel 3.

End point type	Secondary

End point timeframe:

Baseline, Week 40

End point values	Panel 1	Panel 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	9		
Units: percentage change of HBcAg + Hepatocytes				
median (inter-quartile range (Q1-Q3))	-54.49 (-87.02 to -42.26)	0.03 (0.00 to 0.04)		

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 1 and 2: Change From Baseline in Percentage of Intrahepatic Viral Parameter: Covalently Closed Circular Deoxyribonucleic Acid Positive (cccDNA+)

Hepatocytes at Week 40

End point title	Panel 1 and 2: Change From Baseline in Percentage of Intrahepatic Viral Parameter: Covalently Closed Circular Deoxyribonucleic Acid Positive (cccDNA+) Hepatocytes at Week 40[15]

End point description:

Change from baseline in percentage of intrahepatic viral parameters: cccDNA positive hepatocytes were reported. The percentage of cccDNA-positive hepatocytes, were derived as number of cccDNA positive hepatocytes*100 per total number of evaluated hepatocytes. ITT population included subjects who were randomly assigned or enrolled to an intervention arm and received at least 1 dose of intervention. Subjects were analyzed according to study intervention they were randomly assigned or enrolled. Here "N" (Number of subjects analyzed) signifies the number of subjects that were evaluable for this endpoint. Data for this endpoint was not planned to be collected and analyzed for Panel 3.

End point type	Secondary

End point timeframe:

Baseline, Week 40

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: Data for this endpoint was not planned to be collected and analyzed for Panel 3.

End point values	OL Phase: Panel 1	OL Phase: Panel 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: percentage change of cccDNA+ hepatocytes				
median (inter-quartile range (Q1-Q3))	-4.50 (-40.88 to 12.97)	-2.40 (-22.84 to 7.57)		

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 1 and 2: Change From Baseline in Percentage of Intrahepatic Viral Parameter: HBsAg Positive (HBsAg+) Hepatocytes at Week 40

End point title	Panel 1 and 2: Change From Baseline in Percentage of Intrahepatic Viral Parameter: HBsAg Positive (HBsAg+) Hepatocytes at Week 40[16]

End point description:

Change from baseline in percentage of intrahepatic viral parameter: HBsAg positive hepatocytes at Week 40 were reported. The percentage of HBsAg positive hepatocytes were derived as number of HBsAg positive hepatocytes * 100 per total number of evaluated hepatocytes. ITT population included subjects who were randomly assigned or enrolled to an intervention arm and received at least 1 dose of intervention. Subjects were analyzed according to study intervention they were randomly assigned or enrolled. Here "N" (Number of subjects analyzed) signifies the number of subjects that were evaluable for this endpoint. Data for this endpoint was not planned to be collected and analyzed for Panel 3.

End point type	Secondary

End point timeframe:

Baseline, Week 40

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: Data for this endpoint was not planned to be collected and analyzed for Panel 3.

End point values	OL Phase: Panel 1	OL Phase: Panel 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	9		
Units: percentage change of HBsAg+ hepatocytes				
median (inter-quartile range (Q1-Q3))	-92.38 (-95.65 to -73.37)	-14.19 (-21.11 to -7.01)		

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 1 and 2: Change From Baseline in Percentage of Intrahepatic Viral Parameter: Pre-genomic Ribonucleic Acid Positive (pgRNA+) Hepatocytes at Week 40

End point title	Panel 1 and 2: Change From Baseline in Percentage of Intrahepatic Viral Parameter: Pre-genomic Ribonucleic Acid Positive (pgRNA+) Hepatocytes at Week 40[17]

End point description:

Change from baseline in percentage of intrahepatic viral Parameter: pgRNA positive hepatocytes at Week 40 were reported. The percentage of pgRNA-positive hepatocytes were derived as number of pgRNA positive hepatocytes*100 per total number of evaluated hepatocytes. ITT population included subjects who were randomly assigned or enrolled to an intervention arm and received at least 1 dose of intervention. Subjects were analyzed according to study intervention they were randomly assigned or enrolled. Here "N" (Number of subjects analyzed) signifies the number of subjects that were evaluable for this endpoint. Data for this endpoint was not planned to be collected and analyzed for Panel 3.

End point type	Secondary

End point timeframe:

Baseline, Week 40

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: Data for this endpoint was not planned to be collected and analyzed for Panel 3.

End point values	OL Phase: Panel 1	OL Phase: Panel 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: percentage change of pgRNA + hepatocytes				
median (inter-quartile range (Q1-Q3))	-81.23 (-86.19 to -74.14)	-6.74 (-15.81 to -2.01)		

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 1 and 2: Change From Baseline in Transcriptional Activity (Ratio of pg RNA/cccDNA) at Week 40

End point title	Panel 1 and 2: Change From Baseline in Transcriptional Activity

	(Ratio of pg RNA/cccDNA) at Week 40[18]

End point description:

Change from baseline in transcriptional activity (ratio of pgRNA/cccDNA) at Week 40 were reported. ITT population included subjects who were randomly assigned or enrolled to an intervention arm and received at least 1 dose of intervention. Subjects were analyzed according to study intervention they were randomly assigned or enrolled. Here "N" (Number of subjects analyzed) signifies the number of subjects that were evaluable for this endpoint. Data for this endpoint was not planned to be collected and analyzed for Panel 3.

End point type	Secondary

End point timeframe:

Baseline, Week 40

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: Data for this endpoint was not planned to be collected and analyzed for Panel 3.

End point values	OL Phase: Panel 1	OL Phase: Panel 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: ratio				
median (inter-quartile range (Q1-Q3))	50.00 (49.07 to 58.83)	8.86 (-3.03 to 27.45)		

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 1, 2: Change From Baseline in Percentage of Intrahepatic Viral Parameter: Silent Infected Hepatocytes at Week 40

End point title	Panel 1, 2: Change From Baseline in Percentage of Intrahepatic Viral Parameter: Silent Infected Hepatocytes at Week 40[19]

End point description:

Change from baseline in percentage of intrahepatic viral parameter: silent infected hepatocytes (that is infected hepatocytes without HBV transcription; cccDNA-positive/HBV RNA-negative hepatocytes) at Week 40 were reported. The percentage of silent infected hepatocytes (SIH), were derived as number of silent infected hepatocytes*100 per total number of evaluated hepatocytes. ITT population included subjects who were randomly assigned or enrolled to an intervention arm and received at least 1 dose of intervention. Subjects were analyzed according to study intervention they were randomly assigned or enrolled. Here "N" (Number of subjects analyzed) signifies the number of subjects that were evaluable for this endpoint. Data for this endpoint was not planned to be collected and analyzed for Panel 3.

End point type	Secondary

End point timeframe:

Baseline, Week 40

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: Data for this endpoint was not planned to be collected and analyzed for Panel 3.

End point values	OL Phase: Panel 1	OL Phase: Panel 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: percent change of hepatocytes				
median (inter-quartile range (Q1-Q3))	25.06 (21.40 to 31.63)	2.88 (-14.74 to 8.80)		

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 1, 2 and 3: Percentage of Subjects With HBsAg Seroclearance at Week 72 Without Restarting Nucleos(t)Ide Analog (NA) Treatment

End point title	Panel 1, 2 and 3: Percentage of Subjects With HBsAg Seroclearance at Week 72 Without Restarting Nucleos(t)Ide Analog (NA) Treatment

End point description:

Percentage of subjects with HBsAg seroclearance (defined as HBsAg < LLOQ: 0.05 IU/mL) at Week 72 without restarting NA treatment were reported. ITT population included subjects who were randomly assigned or enrolled to an intervention arm and received at least 1 dose of intervention. Subjects were analyzed according to study intervention they were randomly assigned or enrolled. Here "N" (Number of subjects analyzed) signifies the number of subjects that were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

At Week 72 (24 weeks after completion of all study drugs at Week 48)

End point values	Follow-up Phase: Panel 1	Follow-up Phase: Panel 2	Follow-up Phase: Panel 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	10	4	
Units: Percentage of subjects				
number (not applicable)	0	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 1, 2 and 3: Percentage of Subjects With Sustained (Reduction) Serum HBsAg Response Per Definition 1 at Follow-up Week 48

End point title	Panel 1, 2 and 3: Percentage of Subjects With Sustained (Reduction) Serum HBsAg Response Per Definition 1 at Follow-up Week 48

End point description:

Percentage of subjects with sustained (reduction) serum HBsAg response per Definition 1 at follow-up Week 48 were reported. Sustained serum HBsAg response per definition 1 was defined as: for subjects with data for last follow-up visit (Follow-up Week 48 for subjects who did not receive PegIFN-alpha2a or received PegIFN-alpha2a and did not meet NA completion criteria, and last Follow-up visit for subjects who received PegIFN-alpha2a and stopped NA during Follow-up): subjects who had a >1 log decline in

HBsAg response at last scheduled follow-up visit and had an HBsAg <1000 IU/mL at last scheduled follow-up visit, or for subjects without data at last follow-up visit: HBsAg values had a >2 log decline at second most recent visit or >1.5 log decline at latest visit (most recent value used) compared to baseline and had an HBsAg <1000 IU/mL at last available timepoint. ITT population analyzed. Subjects were analysed according to study intervention they were randomly assigned or enrolled.

End point type	Secondary

End point timeframe:

Follow-up Week 48

End point values	Follow-up Phase: Panel 1	Follow-up Phase: Panel 2	Follow-up Phase: Panel 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	10	4	
Units: Percentage of subjects				
arithmetic mean (confidence interval 80%)	50.0 (26.73 to 73.27)	70.0 (44.83 to 88.42)	50.0 (14.26 to 85.74)	

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 1, 2 and 3: Percentage of Subjects With Sustained (Reduction) Serum HBsAg Response Per Definition 2 at Follow-up Week 48

End point title	Panel 1, 2 and 3: Percentage of Subjects With Sustained (Reduction) Serum HBsAg Response Per Definition 2 at Follow-up Week 48

End point description:

Percentage of subjects with sustained (reduction) serum HBsAg response per Definition 2 at follow-up Week 48 were reported. Sustained serum HBsAg response per definition 2 was defined as: for subjects with a >1 log decline in HBsAg from baseline at last follow up visit: Among the most recent three visits, the difference between log HBsAg at 2 of 3 last visit and 1 of 3 last visit is <0.2, and the difference between log HBsAg at 3 of 3 last visit and 1 of 3 last visit is <0.2. ITT population included subjects who were randomly assigned or enrolled to an intervention arm and received at least 1 dose of intervention. Subjects were analyzed according to study intervention they were randomly assigned or enrolled. Here "N" (Number of subjects analyzed) signifies the number of subjects that were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Follow-up Week 48

End point values	Follow-up Phase: Panel 1	Follow-up Phase: Panel 2	Follow-up Phase: Panel 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	7	2	
Units: Percentage of subjects				
arithmetic mean (confidence interval 80%)	50.0 (23.97 to 76.03)	42.9 (16.96 to 72.14)	50.0 (5.13 to 94.87)	

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 1, 2 and 3: Percentage of Subjects Who Achieved HBeAg Seroclearance

End point title	Panel 1, 2 and 3: Percentage of Subjects Who Achieved HBeAg Seroclearance

End point description:

Percentage of subjects who achieved HBeAg Seroclearance were reported. HBeAg seroclearance was defined as (quantitative) HBeAg <LLOQ (<0.11 IU/mL). ITT population included subjects who were randomly assigned or enrolled to an intervention arm and received at least 1 dose of intervention. Subjects were analyzed according to study intervention they were randomly assigned or enrolled. Here "N" (Number of subjects analyzed) signifies the number of subjects that were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Follow-up Week 48

End point values	Follow-up Phase: Panel 1	Follow-up Phase: Panel 2	Follow-up Phase: Panel 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	10	4	
Units: percentage of Subjects				
number (not applicable)	25.0	20.0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 1, 2 and 3: Percentage of SubjectsWith Sustained (Reduction) Serum HBsAg Response Per Definition 4 at Follow-up Week 48

End point title	Panel 1, 2 and 3: Percentage of SubjectsWith Sustained (Reduction) Serum HBsAg Response Per Definition 4 at Follow-up Week 48

End point description:

Percentage of subjects with sustained (reduction) serum HBsAg response per definition 4 follow-up Week 48 were reported. Sustained serum HBsAg response per definition 4 were classified into 3 categories with respect to the difference between HBsAg level at the last Follow-up timepoint and end of treatment: Increase: >+0.2 log10 IU/mL , stable: within plus or minus (+/-) 0.2 log10 IU/mL, and decrease: >-0.2 log10 IU/mL. ITT population included subjects who were randomly assigned or enrolled to an intervention arm and received at least 1 dose of intervention. Subjects were analyzed according to study intervention they were randomly assigned or enrolled. Here "N" (Number of subjects analyzed) signifies the number of subjects that were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Follow-up Week 48

End point values	Follow-up Phase: Panel 1	Follow-up Phase: Panel 2	Follow-up Phase: Panel 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	10	4	
Units: Percentage of subjects				
number (not applicable)				
Stable: Within +/-0.2 log10	11.1	0	0	
Decrease: > -0.2 log10 IU/mL	22.2	30.0	25.0	
Increase: > +0.2 log10 IU/mL	66.7	70.0	75.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 1, 2 and 3: Percentage of Subjects With Sustained (Reduction) Serum HBsAg Response Per Definition 3 at Follow-up Week 48

End point title	Panel 1, 2 and 3: Percentage of Subjects With Sustained (Reduction) Serum HBsAg Response Per Definition 3 at Follow-up Week 48

End point description:

Percentage of subjects with sustained (reduction) serum HBsAg response per Definition 3 at follow-up Week 48 were reported. Sustained serum HBsAg response per definition 3 for subjects with a >1 log decline in HBsAg from baseline at last follow up visit: Among the most recent three visits, the difference between log HBsAg at 2 of 3 last visit and 1 of 3 last visit is <0.2, and the difference between log HBsAg at 3 of 3 last visit and 1 of 3 last visit is <0.2 and have an HBsAg <1000 IU/mL at the last available timepoint. ITT population included subjects who were randomly assigned or enrolled to an intervention arm and received at least 1 dose of intervention. Subjects were analyzed according to study intervention they were randomly assigned or enrolled. Here "N" (Number of subjects analyzed) signifies the number of subjects that were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From follow-up Week 24 up to follow-up Week 48

End point values	Follow-up Phase: Panel 1	Follow-up Phase: Panel 2	Follow-up Phase: Panel 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	7	2	
Units: Percentage of subjects				
number (confidence interval 80%)	25.0 (6.86 to 53.82)	42.9 (16.96 to 72.14)	50.0 (5.13 to 94.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 1, 2 and 3: Percentage of Subjects Who Achieved HBsAg Seroconversion

End point title	Panel 1, 2 and 3: Percentage of Subjects Who Achieved HBsAg Seroconversion

End point description:

Seroconversion of HBsAg was defined as having achieved HBsAg seroclearance (defined as quantitative HBsAg <LLOQ [<0.05 IU/mL]) and appearance of anti-HBs antibodies (defined as a baseline anti-HBs antibodies [quantitative] <LLOQ [<5 milli-international units per milliliter {mIU/mL}] and a post-baseline assessment >=LLOQ [>=5 mIU/mL]). ITT population included subjects who were randomly assigned or enrolled to an intervention arm and received at least 1 dose of intervention. Subjects were analyzed according to study intervention they were randomly assigned or enrolled. Here, 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (Day 1) up to follow-up Week 48

End point values	OL Phase: Panel 1	OL Phase: Panel 2	OL Phase: Panel 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	7	2	
Units: Percentage of subjects				
number (not applicable)	28.6	11.1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 1, 2 and 3: Percentage of Subjects who Achieved HBeAg Seroclearance

End point title	Panel 1, 2 and 3: Percentage of Subjects who Achieved HBeAg Seroclearance

End point description:

Percentage of subjects who achieved HBeAg Seroclearance were reported. HBeAg seroclearance was defined as (quantitative) HBeAg <LLOQ (<0.11 IU/mL). ITT population included subjects who were randomly assigned or enrolled to an intervention arm and received at least 1 dose of intervention. Subjects were analyzed according to study intervention they were randomly assigned or enrolled. Here "N" (Number of subjects analyzed) signifies the number of subjects that were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Follow-up Week 48

End point values	Follow-up Phase: Panel 1	Follow-up Phase: Panel 2	Follow-up Phase: Panel 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	9	4	
Units: percentage of subjects				
number (not applicable)	37.5	100.0	75.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 1, 2 and 3: Percentage of Subjects With Off-treatment Virologic Flares per Derivation 1

End point title	Panel 1, 2 and 3: Percentage of Subjects With Off-treatment Virologic Flares per Derivation 1

End point description:

Virologic flare (VF) per derivation 1 was defined only for subjects who were off-treatment [OFT: period after stopping all study drugs, including NA] and who had HBV DNA<LLOQ (<20 IU/mL) at last observed point on-treatment [OT]); start date [SD] of confirmed VF was first date of 2 consecutive visits with HBV DNA >200 IU/mL. End date [ED] of same confirmed VF was first date when HBV DNA value returns to <=200 IU/mL or date of NA restart, whichever comes first. Each virologic flare were categorized based on confirmed (that is, 2 consecutive values) peak HBV DNA above any of 3 thresholds within the start and end date of that flare as followed: 20,000 IU/mL, 2,000 IU/mL, and 200 IU/mL. Subjects were counted only once for any given flare, regardless of the number of times they actually experienced the flare. ITT set were analysed. Here "N" (Subjects analysed) signifies subjects evaluable for this endpoint. 99999 signifies that no subjects were available for the analysis.

End point type	Secondary

End point timeframe:

From baseline (Day 1) up to follow-up Week 48

End point values	OL Phase: Panel 1	OL Phase: Panel 2	OL Phase: Panel 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[20]	3	2	
Units: percentage of subjects				
number (not applicable)				
HBV DNA > 200 IU/mL		0	0	
HBV DNA > 2,000 IU/mL		33.3	0	
HBV DNA > 20,000 IU/mL		0	50.0	

Notes:

[20] - N=0 signifies that data were not collected and analyzed for this arm.

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 1, 2 and 3: Percentage of Subjects who Achieved HBeAg Seroconversion

End point title	Panel 1, 2 and 3: Percentage of Subjects who Achieved HBeAg Seroconversion

End point description:

Percentage of subjects who achieved HBeAg seroconversion were reported. Seroconversion of HBeAg was defined as having achieved HBeAg seroclearance (defined as [quantitative] HBeAg <LLOQ [<0.11 IU/mL]) together with appearance of anti-HBe antibodies (defined as a baseline anti-HBe antibodies [qualitative] with a "negative" result and a post-baseline assessment with “positive” result). ITT population included subjects who were randomly assigned or enrolled to an intervention arm and received at least 1 dose of intervention. Subjects were analyzed according to study intervention they were randomly assigned or enrolled. Here "N" (Number of subjects analyzed) signifies the number of subjects that were evaluable for this endpoint. Here 99999 signifies that no subject was available for the analysis.

End point type	Secondary

End point timeframe:

From baseline (Day 1) up to follow-up Week 48

End point values	OL Phase: Panel 1	OL Phase: Panel 2	OL Phase: Panel 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	0[21]	2	
Units: Percentage of subjects				
number (not applicable)	28.6		50.0	

Notes:

[21] - Here N=0 signifies that data were not collected and analyzed for this arm.

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 1, 2 and 3: Percentage of Subjects With Off-treatment and On-treatment Biochemical Flares

End point title	Panel 1, 2 and 3: Percentage of Subjects With Off-treatment and On-treatment Biochemical Flares

End point description:

Off-treatment biochemical flare was defined as first date of 2 consecutive visits with ALT and/or AST >=3*ULN and >=3*nadir while subject received no study drugs. End date of same off-treatment biochemical flare =first date with 50 % reduction from peak ALT and/or AST level & <3*ULN. On-treatment (time period during which the subject received any of study drugs) biochemical flare =first date of 2 consecutive visits with ALT and/ or AST >=3*ULN and >=3*nadir (lowest value observed up to start of flare) while subject was on-treatment. End date of same on-treatment biochemical flare =first date with a 50% reduction from the peak ALT and/or AST level and <3*ULN, regardless of stopping study drugs. Subjects were counted only once for any given flare, regardless of the number of times they actually experienced flare. ITT Population. Here, "n"=number of subjects analyzed at specified categories and 99999 signifies that no subject was available for the analysis at the specified category.

End point type	Secondary

End point timeframe:

From baseline (Day 1) up to follow-up Week 48

End point values	Panel 1	Panel 2	Panel 3	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	10	10	
Units: Percentage of subjects				
number (not applicable)				
Off-treatment biochemical flare (n=0, 3, 2)	99999	0	0	
On-treatment biochemical flare (n=10, 10, 4)	10.0	10.0	25.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 1, 2 and 3: Percentage of Subjects With Off-treatment Clinical Flares

End point title	Panel 1, 2 and 3: Percentage of Subjects With Off-treatment Clinical Flares

End point description:

Clinical flares occurred either when a virologic flare and biochemical flare overlapped in time or when a biochemical flare started within 4 weeks following the end of a virologic flare. Off-treatment was defined as the time period after stopping all study drugs (including NA). The start date of a clinical flare was the minimum start date of the virologic flare and biochemical flare. The end date of a clinical flare was the maximum end date of the virologic flare and biochemical flare, that is, the later date between HBV DNA returned to <=200 IU/mL (or <=1 log10) and 50 %reduction from the peak ALT and/or AST level and <3*ULN reached during the biochemical flare. Subjects were counted only once for any given flare, regardless of the number of times they actually experienced the flare. ITT Population. Here, "n"=number of subjects analyzed at specified categories and 99999 signifies that no subject was available for the analysis at the specified category.

End point type	Secondary

End point timeframe:

From baseline (Day 1) up to follow-up Week 48

End point values	Panel 1	Panel 2	Panel 3	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[22]	3	2	
Units: percentage of subjects				
number (not applicable)				
HBV DNA >200 IU/mL (n=0, 3, 2)		0	0	
HBV DNA >2,000 IU/mL (n=0, 3, 2)		0	0	
HBV DNA >20,000 IU/mL (n=0, 3, 2)		0	50.0	

Notes:

[22] - N=0 signifies that no subjects were available for the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 1, 2 and 3: Percentage of Subjects With Virologic Breakthrough

End point title	Panel 1, 2 and 3: Percentage of Subjects With Virologic Breakthrough

End point description:

Virological breakthrough was defined as having a confirmed on-treatment HBV DNA increase by >1 log10 IU/mL from nadir level (lowest level reached during treatment) in subjects who did not have on-treatment HBV DNA level < LLOQ (<20 IU/mL) or confirmed on-treatment HBV DNA level >200 IU/mL in subjects who had on-treatment HBV DNA level <LLOQ (<20 IU/mL) of the HBV DNA assay. Confirmed HBV DNA increase/level means that the criterion should be fulfilled at 2 or more consecutive time points or at the last observed on-treatment time point. On treatment was defined as the time period in which the subject received any of the study interventions (JNJ-3989 and/or JNJ 6379 and/or NA and/or PegIFN-alpha2a). ITT population included subjects who were randomly assigned or enrolled to an intervention arm and received at least 1 dose of intervention. Subjects were analyzed according to study intervention they were randomly assigned or enrolled.

End point type	Secondary

End point timeframe:

From baseline (Day 1) up to follow-up Week 48

End point values	OL Phase: Panel 1	OL Phase: Panel 2	OL Phase: Panel 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	10	4	
Units: Percentage of subjects				
number (confidence interval 80%)	0 (0.00 to 20.57)	0 (0.00 to 20.57)	0 (0.00 to 43.77)	

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 1, 2 and 3: Time to Achieve First HBsAg Seroclearance

End point title	Panel 1, 2 and 3: Time to Achieve First HBsAg Seroclearance

End point description:

Time to first occurrence of HBsAg seroclearance (defined as quantitative HBsAg <LLOQ [<0.05 IU/mL]) were reported. Time to first occurrence of 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. Subjects who withdrew early from the study before achieving HBsAg seroclearance or who did not achieve HBsAg seroclearance were censored at the last available HBsAg assessment. Kaplan-Meier method was used for estimation. ITT population included subjects who were randomly assigned or enrolled to an intervention arm and received at least 1 dose of intervention. Subjects were analyzed according to study intervention they were randomly assigned or enrolled. Here, 99999 signifies that median and 80% CI data were not estimable due to insufficient number of subjects with events.

End point type	Secondary

End point timeframe:

From baseline (Day 1) up to follow-up Week 48

End point values	OL Phase: Panel 1	OL Phase: Panel 2	OL Phase: Panel 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	10	4	
Units: weeks				
median (full range (min-max))	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 1, 2 and 3: Number of Subjects With HBV-Specific Peripheral Blood T-cell Responses

End point title	Panel 1, 2 and 3: Number of Subjects With HBV-Specific Peripheral Blood T-cell Responses

End point description:

Number of subjects with HBV-specific peripheral blood T-cell responses were reported. HBV-specific T-cells were characterized in peripheral blood mononuclear cell immune analysis by binding assays (multimer staining) combined with downstream T-cell responses and transcriptome profiling. ITT population included subjects who were randomly assigned or enrolled to an intervention arm and received at least 1 dose of intervention. Here "N" (Number of subjects analyzed) signifies the number of subjects that were evaluable for this endpoint and "n"=number of subjects analyzed at specified categories and 99999 signifies that no subject was available for the analysis at the specified category.

End point type	Secondary

End point timeframe:

Open-label phase: Weeks 40, 44, and 48; Follow-up Phase: Follow-up Weeks 2, 12 and 24

End point values	OL Phase: Panel 1	Follow-up Phase: Panel 1	OL Phase: Panel 2	Follow-up Phase: Panel 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	9	7	10
Units: Subjects				
Open Label: Week 40 (n= 7, 7, 1, 0, 0, 0)	6	0	6	0
Open Label: Week 44 (n= 1, 1,0, 0, 0, 0)	0	0	1	0
Open Label: Week 48 (n=1, 0, 0, 0, 0, 0)	1	0	99999	0
Follow-up Week 2 (n=0, 0, 0, 8, 10, 3)	0	4	0	10
Follow-up Week 12 (n= 0, 0, 0, 8, 10, 3)	0	1	0	5
Follow-up Week 24 (n= 0, 0, 0, 9, 9, 4)	0	5	0	9

End point values	OL Phase: Panel 3	Follow-up Phase: Panel 3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	4		
Units: Subjects				

Open Label: Week 40 (n= 7, 7, 1, 0, 0, 0)	0	0		
Open Label: Week 44 (n= 1, 1,0, 0, 0, 0)	99999	0		
Open Label: Week 48 (n=1, 0, 0, 0, 0, 0)	99999	0		
Follow-up Week 2 (n=0, 0, 0, 8, 10, 3)	0	3		
Follow-up Week 12 (n= 0, 0, 0, 8, 10, 3)	0	2		
Follow-up Week 24 (n= 0, 0, 0, 9, 9, 4)	0	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 1, 2 and 3: Percentage of Subjects With Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (TESAEs)

End point title	Panel 1, 2 and 3: Percentage of Subjects With Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (TESAEs)

End point description:

Percentage of subjects with TEAES (including serious and non-serious) and TESAEs were reported. An AE was any untoward medical occurrence in a clinical study subject administered a medicinal (investigational or non-investigational) product. An AE does not necessarily have a causal relationship with the intervention. Any AE occurring at or after the initial administration of study intervention was considered to be treatment emergent. 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 subjectswho 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:

Open-label: Day 1 (Week 0) up to Week 48; Follow-up Phase: Follow-up Week 1 up to follow-up Week 48

End point values	OL Phase: Panel 1	Follow-up Phase: Panel 1	OL Phase: Panel 2	Follow-up Phase: Panel 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	10	10
Units: Percentage of subjects				
number (not applicable)				
TEAES	90.0	50.0	100.0	60.0
TESAES	10.0	0	0	0

End point values	OL Phase: Panel 3	Follow-up Phase: Panel 3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: Percentage of subjects				

number (not applicable)				
TEAES	75.0	75.0		
TESAES	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 1, 2 and 3: Percentage of Subjects With Worst (Grade 3 and 4) Treatment-emergent Division of Acquired Immunodeficiency Syndrome (DAIDS) Toxicity Grade in Clinical Laboratory Tests

End point title	Panel 1, 2 and 3: Percentage of Subjects With Worst (Grade 3 and 4) Treatment-emergent Division of Acquired Immunodeficiency Syndrome (DAIDS) Toxicity Grade in Clinical Laboratory Tests

End point description:

Clinical laboratory test parameters were Hematology : absolute neutrophil count (ANC); Chemistry : alanine aminotransferase (ALT) and serum glutamic pyruvic transaminase (SGPT), aspartate aminotransferase(AST) or serum glutamic oxaloacetic transaminase (SGOT), amylase (pancreatic and total), creatinine Kinase, creatinine, low-density lipoprotein (LDL), lipase, estimated glomerular filtration rate (eGFR) on serum creatinine (Cr). DAIDS toxicity grades (Gd) were Grade 1 (Mild), Grade 2 (Moderate), Grade 3 (Severe), Grade 4 (Potentially Life-Threatening). Percentage of subjects with treatment-emergent DAIDS toxicity Grade 3 or 4 were reported in this endpoint. For toxicity grades, treatment-emergent was concluded if the postbaseline grade was worse than the baseline grade. Only those abnormality with at least one subject were reported. Safety analysis set. Subjects were analyzed as per study intervention they actually received. "n"=number of subjects analyzed at specified categories.

End point type	Secondary

End point timeframe:

Open-label phase: From Day 1 (Week 0) up to Week 48; Follow-up Phase: Follow-up Week 1 up to follow-up Week 48

End point values	OL Phase: Panel 1	Follow-up Phase: Panel 1	OL Phase: Panel 2	Follow-up Phase: Panel 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	10	10
Units: Percentage of subjects				
number (not applicable)				
Hem: ANC: Low: Grade 3 (n=9, 10, 4, 10, 10, 4)	0	0	10.0	10.0
ALT or SGPT: High: Gd 3 (n= 9, 10, 4, 10, 10, 4)	0	10.0	10.0	10.0
ALT or SGPT: High: Gd 4 (n=9, 10, 4, 10, 10,4)	0	0	0	0
AST/SGOT: High: Gd 3 (n=9,10,4,10,10,4)	0	0	10.0	0
Amylase (Pancreatic): High: Gd 4 (n=4,5,4,4,5,3)	25.0	0	0	0
Amylase (Total): High:Grade 3 (n=9,10,4,9,10,4)	11.1	0	0	0
Creatinine Kinase-High: Gd 3 (n=9,10,4,10,10,4)	0	0	0	0

Creatinine Kinase :High: Gd 4 (n=9,10,4,10,10,4)	0	0	10.0	0
Creatinine: High: Gd 3 (n=9, 10, 4, 10, 10, 4)	11.1	0	0	0
LDL (Fasting):High: Gd 3 (n=9,10,4,10,10,4)	0	0	10.0	0
Lipase: High: Gd 3 (n=9, 10, 4, 9, 10, 4)	0	0	10.0	0
eGFR Cr: Low: Gd 3 (n=9, 10, 4 10, 10, 4)	0	0	10.0	0

End point values	OL Phase: Panel 3	Follow-up Phase: Panel 3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: Percentage of subjects				
number (not applicable)				
Hem: ANC: Low: Grade 3 (n=9, 10, 4, 10, 10, 4)	25.0	25.0		
ALT or SGPT: High: Gd 3 (n= 9, 10, 4, 10, 10, 4)	25.0	0		
ALT or SGPT: High: Gd 4 (n=9, 10, 4, 10, 10,4)	0	25.0		
AST/SGOT: High: Gd 3 (n=9,10,4,10,10,4)	0	25.0		
Amylase (Pancreatic): High: Gd 4 (n=4,5,4,4,5,3)	0	0		
Amylase (Total): High:Grade 3 (n=9,10,4,9,10,4)	0	0		
Creatinine Kinase-High: Gd 3 (n=9,10,4,10,10,4)	25.0	0		
Creatinine Kinase :High: Gd 4 (n=9,10,4,10,10,4)	0	0		
Creatinine: High: Gd 3 (n=9, 10, 4, 10, 10, 4)	0	0		
LDL (Fasting):High: Gd 3 (n=9,10,4,10,10,4)	0	0		
Lipase: High: Gd 3 (n=9, 10, 4, 9, 10, 4)	0	0		
eGFR Cr: Low: Gd 3 (n=9, 10, 4 10, 10, 4)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 1, 2 and 3: Percentage of Subjects With Worst (Abnormally Low/High)Treatment-emergent DAIDS Toxicity Grade in Electrocardiogram (ECG)

End point title	Panel 1, 2 and 3: Percentage of Subjects With Worst (Abnormally Low/High)Treatment-emergent DAIDS Toxicity Grade in Electrocardiogram (ECG)

End point description:

ECG parameters included ECG mean heart rate (HR)(beats per minute[bpm]), Pulse rate (PR) interval (milliseconds [ms]), QRS duration (ms) and QTc Corrected (Fridericia's formula QTcF). Abnormalities

were graded as follows: ECG mean heart rate (abnormally low HR <45 bpm) and (abnormally high HR>=120 bpm); PR interval (abnormally high >220 ms) and QPRS (abnormally high >=120 ms); OT interval corrected for heart rate according to Fridericia (QTcF); borderline prolonged (BRD Pr)QTc (>=450 to <=480 ms), prolonged QTc (>=480 to <=500 ms)and pathologically prolonged QTc (>500 ms). For worst abnormality, treatment-emergent was concluded if the abnormality worsened as compared to the abnormality at baseline: abnormally high to abnormally low and vice-versa. Only those abnormality with at least one subject had data were reported. Safety analysis set. Subjects were analyzed as per study intervention they actually received. "n"=number of subjects analyzed at specified categories.

End point type	Secondary

End point timeframe:

Open-label phase: From Day 1 (Week 0) up to Week 48; Follow-up Phase: Follow-up Week 1 up to follow-up Week 48

End point values	OL Phase: Panel 1	Follow-up Phase: Panel 1	OL Phase: Panel 2	Follow-up Phase: Panel 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	9	10	10
Units: Percentage of subjects				
number (not applicable)				
ECG Mean HR: low (<45 bpm) (n=9, 10, 4, 9, 10, 4)	0	0	10.0	10.0
PR:Aggregate(Agg):High:>220 ms:(n=9,10,4,9,10,4)	11.1	11.1	20.0	20.0
QTcF:Agg:BRD Pr:>=450to<=480 ms:(n=9,10,4,9,10,4)	0	0	10.0	0

End point values	OL Phase: Panel 3	Follow-up Phase: Panel 3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: Percentage of subjects				
number (not applicable)				
ECG Mean HR: low (<45 bpm) (n=9, 10, 4, 9, 10, 4)	0	0		
PR:Aggregate(Agg):High:>220 ms:(n=9,10,4,9,10,4)	0	0		
QTcF:Agg:BRD Pr:>=450to<=480 ms:(n=9,10,4,9,10,4)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 1, 2 and 3: Percentage of Subjects With Worst (Abnormally Low/High) Treatment-emergent DAIDS Toxicity Grade in Vital Signs

End point title	Panel 1, 2 and 3: Percentage of Subjects With Worst (Abnormally Low/High) Treatment-emergent DAIDS Toxicity Grade in Vital Signs

End point description:

Percentage of subjects with worst treatment-emergent DAIDS toxicity grade in vital signs were reported. Abnormality grades were: pulse rate (abnormally low <=45 bpm) and (abnormally high >=120 bpm). An assessment was treatment-emergent if abnormality worsened as compared to the abnormality at baseline: from abnormally high to abnormally low and vice-versa. Only the category (pulse rate) in which at least one subject had data 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. Here "N" (Number of subjects analyzed) signifies subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Open-label phase: From Day 1 (Week 0) up to Week 48; Follow-up Phase: Follow-up Week 1 up to follow-up Week 48

End point values	OL Phase: Panel 1	Follow-up Phase: Panel 1	OL Phase: Panel 2	Follow-up Phase: Panel 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	10	10
Units: Percentage of subjects				
number (not applicable)	0	0	10.0	0

End point values	OL Phase: Panel 3	Follow-up Phase: Panel 3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: Percentage of subjects				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 1, 2 and 3: Number of Subjects With Clinically Significant Treatment-emergent Abnormalities in Physical Examination

End point title	Panel 1, 2 and 3: Number of Subjects With Clinically Significant Treatment-emergent Abnormalities in Physical Examination

End point description:

Number of subjects with clinically significant treatment-emergent abnormalities in physical examination were reported. Physical examination included head/neck/thyroid, eyes/ears/nose/throat, respiratory, cardiovascular, lymph nodes, abdomen, skin, musculoskeletal, and neurological examinations. 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:

Open-label phase: From Day 1 (Week 0) up to Week 48; Follow-up Phase: Follow-up Week 1 up to follow-up Week 48

End point values	OL Phase: Panel 1	Follow-up Phase: Panel 1	OL Phase: Panel 2	Follow-up Phase: Panel 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	10	10
Units: Subjects	4	0	0	0

End point values	OL Phase: Panel 3	Follow-up Phase: Panel 3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 2 and 3: Plasma Trough Concentration (C[0hour]) of JNJ-73763989 (JNJ-73763976, JNJ-73763924)

End point title	Panel 2 and 3: Plasma Trough Concentration (C[0hour]) of JNJ-73763989 (JNJ-73763976, JNJ-73763924)[23]

End point description:

Plasma trough concentration (C[0hour]) of JNJ-73763989 (JNJ-73763976, JNJ-73763924) were reported. C0h was the pre-dose plasma concentration of the JNJ-73763989 (JNJ-73763976, JNJ-73763924). Non-compartmental analysis were conducted to analyze plasma concentration of JNJ-73763989 and its molecules. Pharmacokinetics (PK) analysis which included subjects of Panel 2 and Panel 3 who had consented to participate in the intensive PK subgroup were analyzed. Data for this endpoint was planned to be collected and analyzed for Panel 2 and 3 alone. Here, "99999" signifies that mean and standard deviation were not calculable because sample concentration was below quantification limit (that is <2.1 ng/mL)..

End point type	Secondary

End point timeframe:

Week 4 : Pre-dose on Day 29

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: Data for this endpoint was planned to be collected and analyzed for Panel 2 and 3 alone.

End point values	OL Phase: Panel 2	OL Phase: Panel 3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	4		
Units: nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
C0hJNJ-73763976	99999 (± 99999)	99999 (± 99999)		

C0h-JNJ-73763924	99999 (± 99999)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 2 and 3: Maximum Observed Plasma Concentration (Cmax) of JNJ-73763989 (JNJ-73763976, JNJ-73763924)

End point title	Panel 2 and 3: Maximum Observed Plasma Concentration (Cmax) of JNJ-73763989 (JNJ-73763976, JNJ-73763924)[24]

End point description:

Maximum observed plasma concentration (Cmax) of JNJ-73763989 (JNJ-73763976, JNJ-73763924) were reported. Non-compartmental analysis were conducted to analyze Cmax JNJ-73763989 and its molecules. A PK analysis which included subjects of Panel 2 and Panel 3 who had consented to participate in the intensive PK subgroup were analyzed. Data for this endpoint was planned to be collected and analyzed for Panel 2 and 3 alone. Here, "99999" signifies that data were not collected and analyzed when the subjects available for analysis were less than 3 as planned .

End point type	Secondary

End point timeframe:

Week 4 (Day 29): Pre-dose and 15 minutes, 30 minutes, 1, 2, 3, 4, 6, 8, 10 and 24 hours post dose

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: Data for this endpoint was planned to be collected and analyzed for Panel 2 and 3 alone.

End point values	OL Phase: Panel 2	OL Phase: Panel 3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[25]	4		
Units: Nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Cmax: JNJ-73763976	()	924 (± 428)		
Cmax: JNJ-73763924	()	178 (± 73.1)		

Notes:

[25] - N=0 signifies data were not calculable because a sufficient number of subjects were not available.

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 2 and 3: Minimum Observed Plasma Concentration (Cmin) of JNJ-73763989 (JNJ-73763976, JNJ-73763924)

End point title	Panel 2 and 3: Minimum Observed Plasma Concentration (Cmin) of JNJ-73763989 (JNJ-73763976, JNJ-73763924)[26]

End point description:

Minimum observed plasma concentration (Cmin) of JNJ-73763989 (JNJ-73763976, JNJ-73763924) were reported. Non-compartmental analysis were conducted to analyze Cmin of JNJ-73763989 and its molecules. A PK analysis which included subjects of Panel 2 and Panel 3 who had consented to participate in the intensive PK subgroup were analyzed. Data for this endpoint was planned to be collected and analyzed for Panel 2 and 3 alone. Here, 99999 signifies that mean and standard deviation

were not calculable because sample concentration was below quantification limit (that is <2.1 ng/mL).

End point type	Secondary

End point timeframe:

Week 4 (Day 29): Pre-dose and 15 minutes, 30 minutes, 1, 2, 3, 4, 6, 8, 10 and 24 hours post dose

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: Data for this endpoint was planned to be collected and analyzed for Panel 2 and 3 alone.

End point values	OL Phase: Panel 2	OL Phase: Panel 3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	4		
Units: nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Cmin: JNJ-73763976	99999 (± 99999)	99999 (± 99999)		
Cmin: JNJ-73763924	99999 (± 99999)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 2 and 3:Area Under the Plasma Concentration-time Curve From Time Zero to 24hours (AUC0 to 24h) of JNJ-73763989 (JNJ-73763976, JNJ-73763924)

End point title	Panel 2 and 3:Area Under the Plasma Concentration-time Curve From Time Zero to 24hours (AUC0 to 24h) of JNJ-73763989 (JNJ-73763976, JNJ-73763924)[27]

End point description:

Area under the plasma concentration-time curve from time zero to 24hours (AUC0 to 24h) of JNJ-73763989 (JNJ-73763976, JNJ-73763924) were reported. Non-compartmental analysis were conducted to analyze AUC0 to 24h of JNJ-73763989 and its molecules. A PK analysis which included subjects of Panel 2 and Panel 3 who had consented to participate in the intensive PK subgroup were analyzed. Here, 99999, signifies that data were not collected and analyzed when the subjects available for analysis were less than 3 as planned. Data for this endpoint was planned to be collected and analyzed for Panel 2 and 3 alone.

End point type	Secondary

End point timeframe:

Week 4 (Day 29): Pre-dose and 15 minutes, 30 minutes, 1, 2, 3, 4, 6, 8, 10 and 24 hours post dose

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: Data for this endpoint was planned to be collected and analyzed for Panel 2 and 3 alone.

End point values	OL Phase: Panel 2	OL Phase: Panel 3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[28]	4		
Units: nanograms*hour per milliliters (ng*h/mL)				
arithmetic mean (standard deviation)				
AUC0 to 24h:JNJ-73763976	()	13256 (± 6314)		
AUC0 to 24h: JNJ-73763924	()	2394 (± 1047)		

Notes:

[28] - N=0 signifies data were not calculable because a sufficient number of subjects were not available.

Statistical analyses

No statistical analyses for this end point

Secondary: Panel 2 and 3:Time to Reach the Maximum Observed Plasma Concentration (Tmax) of JNJ-73763989 (JNJ-73763976, JNJ-73763924)

End point title	Panel 2 and 3:Time to Reach the Maximum Observed Plasma Concentration (Tmax) of JNJ-73763989 (JNJ-73763976, JNJ-73763924)[29]

End point description:

Time to reach the maximum observed plasma concentration (tmax) of JNJ-73763989 (JNJ-73763976, JNJ-73763924) were reported. Non-compartmental analysis were conducted to analyze tmax of JNJ-73763989 and its molecules. A PK analysis which included subjects of Panel 2 and Panel 3 who had consented to participate in the intensive PK subgroup were analyzed. Here, 99999, signifies that data were not collected and analyzed when the subjects available for analysis were less than 3 as planned. Data for this endpoint was planned to be collected and analyzed for Panel 2 and 3 alone.

End point type	Secondary

End point timeframe:

Week 4 (Day 29): Pre-dose and 15 minutes, 30 minutes, 1, 2, 3, 4, 6, 8, 10 and 24 hours post dose

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: Data for this endpoint was planned to be collected and analyzed for Panel 2 and 3 alone.

End point values	OL Phase: Panel 2	OL Phase: Panel 3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[30]	4		
Units: hours (h)				
median (full range (min-max))				
tmax: JNJ-73763976	(to)	6.00 (3.00 to 10.00)		
tmax: JNJ-73763924	(to)	5.04 (3.00 to 10.00)		

Notes:

[30] - N=0 signifies data were not calculable because a sufficient number of subjects were not available.

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Open-label phase: From Day 1 (Week 1) up to Week 48; Follow-up Phase: Follow-up Week 1 up to follow-up Week 48

Adverse event reporting additional description:

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.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	OL Phase: Panel 1

Reporting group description:

Prior to PA 5, subjects received either JNJ-3989 200 milligrams (mg) subcutaneous(SC) injection every 4 weeks(Q4W) from Day 1 (Week 1) to Week 44+JNJ-6379 250 mg once daily(QD)+NA (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48 or JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1) to Week 44+NA (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48. After PA 5, subjects stopped JNJ-6379 and continued JNJ-3989+NA. With separate consent, subjects received optional treatment: PegIFN-alpha-2a 180 micrograms(mcg) SC injection once weekly(QW) post Week 40 liver biopsy for either 12 or 24 weeks (anytime between study Week 40 to 72) at investigator's discretion. At end of treatment Week 48, all subjects entered FU phase and stopped JNJ-3989/JNJ-6379 and NA, if NA treatment completion criteria was met as per Week 44 laboratory tests. If NA treatment completion criteria were not met at Week 48, NA was continued till FU phase end (study Week 96).

Reporting group title	OL Phase: Panel 2

Reporting group description:

Prior to PA 5, subjects received either JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1) to Week 44 + JNJ-6379 250 mg QD and NA treatment (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48, or JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1) to Week 44 + NA (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48. After PA 5, subjects discontinued JNJ-6379 and continued JNJ-3989 + NA. With separate consent, subjects received optional treatment with PegIFNalpha-2a 180 mcg SC injection QW after Week 40 liver biopsy for either 12 or 24 weeks (anytime between study Week 40 to 72) at investigator's discretion. At end of treatment Week 48, all subjects entered FU phase and stopped JNJ-3989/JNJ-6379 and NA (if NA treatment completion criteria was met as per Week 44 laboratory tests). If NA treatment completion criteria were not met at Week 48, NA was continued till FU phase end (study Week 96).

Reporting group title	FU Phase: Panel 2

Reporting group description:

After completion of open-label phase (up to 48 weeks) all subjects (with HBeAg negative & virologically suppressed by ETV, TD, or TAF treatment) enrolled prior to PA 5, entered FU phase & stopped all study drugs including NA treatment, but NA treatment continued till end of FU (study Week 96), if NA treatment completion criteria (ALT: <3*ULN, HBV DNA <LLOQ:20 IU/mL, HBeAg negative and HBsAg<10 IU/mL) was not met at Week 48. Subjects who were on treatment with optional PegIFN-alpha-2a 180 mcg SC injection QW after Week 40 liver biopsy but had not met NA treatment completion criteria at Week 48, were assessed at the end of treatment with PegIFN-α2a (study Week 60 or 72) and stopped NA, if the NA treatment completion criteria were met. Subjects who met NA treatment completion criteria (at Week48) were monitored Q4W in FU phase. If NA-retreatment criteria (HBV DNA >20,000 IU/mL, HBV DNA >2,000 IU/mL but <20,000 IU/mL & ALT >5*ULN) was met, NA retreatment was started.

Reporting group title	FU Phase: Panel 1

Reporting group description:

After completion of open-label phase (up to 48 weeks) all subjects (with HBeAg positive and not currently treated) enrolled prior to PA 5, entered FU phase & stopped all study drugs including NA treatment, but NA treatment continued till end of FU (study Week 96), if NA treatment completion criteria (ALT: <3*ULN, HBV DNA <LLOQ:20 IU/mL, HBeAg negative and HBsAg<10 IU/mL) was not met at Week 48. Subjects on treatment with optional PegIFN-alpha-2a 180 mcg SC injection QW after Week 40 liver biopsy but had not met NA treatment completion criteria at Week 48, were assessed at end of treatment with PegIFN-α2a (study Week 60 or 72) and stopped NA, if NA treatment completion criteria

were met. Subjects who met NA treatment completion criteria (at Week 48) were monitored Q4W in FU phase. If NA-retreatment criteria:HBV DNA >20,000 IU/mL, HBV DNA >2,000 IU/mL but <20,000 IU/mL & ALT>5*ULN was met, NA retreatment was started.

Reporting group title	FU Phase: Panel 3

Reporting group description:

After completion of open-label phase (up to 48 weeks) subjects (HBeAg positive or negative & were either not currently treated or virologically suppressed by ETV or TD treatment) enrolled after PA 5, entered FU phase & stopped all study drugs including NA, but NA treatment continued till end of FU (study Week 96), if NA treatment completion criteria ([ALT <3*ULN, HBV DNA <LLOQ; 20 IU/mL, HBeAg negative and HBsAg <10 IU/mL]) was not met at Week 48. Subjects on treatment with optional PegIFNalpha-2a 180 mcg SC injection QW post Week 40 liver biopsy but had not met NA treatment completion criteria at Week 48, were assessed at end of treatment with PegIFN-α2a (study Week 60 or 72) & stopped NA, if NA treatment completion criteria were met. Subjects who met NA treatment completion criteria (at Week 48) were monitored Q4W in FU phase. If NA-retreatment criteria (HBV DNA >20,000 IU/mL, HBV DNA >2,000 IU/mL but <20,000 IU/mL & ALT >5*ULN) was met, NA retreatment was started.

Reporting group title	OL Phase: Panel 3

Reporting group description:

After PA 5, subjects received either JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1 to Week 44) + JNJ-6379 250 mg QD and NA treatment (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48, or JNJ-3989 200 mg SC injection Q4W from Day 1 (Week 1) to Week 44 + NA (ETV 0.5 mg/TD 245 mg/TAF 25 mg) QD from Day 1 (Week 1) to Week 48. After PA 5, subjects discontinued JNJ-6379 and continued JNJ-3989 + NA. With separate consent, subjects received optional treatment with PegIFNalpha-2a 180 mcg SC injection QW after Week 40 liver biopsy for either 12 or 24 weeks (anytime between study Week 40 to 72) at investigator's discretion. At end of treatment Week 48, all subjects entered FU phase and stopped JNJ-3989/JNJ-6379 and NA (if NA treatment completion criteria was met as per Week 44 laboratory tests). If NA treatment completion criteria were not met at Week 48, NA was continued till FU phase end (study Week 96).

Serious adverse events	OL Phase: Panel 1	OL Phase: Panel 2	FU Phase: Panel 2
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (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	FU Phase: Panel 1	FU Phase: Panel 3	OL Phase: Panel 3
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Gastroenteritis			

subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (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

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

Non-serious adverse events	OL Phase: Panel 1	OL Phase: Panel 2	FU Phase: Panel 2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 10 (90.00%)	10 / 10 (100.00%)	6 / 10 (60.00%)
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Influenza Like Illness			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	2 / 10 (20.00%)	2 / 10 (20.00%)	1 / 10 (10.00%)
occurrences (all)	2	2	1
Chills			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Injection Site Bruising			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Injection Site Reaction			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Injection Site Pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Injection Site Erythema			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Pyrexia			

subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	0 / 10 (0.00%)
occurrences (all)	1	3	0
Reproductive system and breast disorders			
Vaginal Haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Nasal Congestion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal Pain			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	2 / 10 (20.00%)
occurrences (all)	2	0	2
Productive Cough			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Mood Swings			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Depressed Mood			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0

Amylase Increased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	7	0	0
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Body Temperature Increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Low Density Lipoprotein Increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Glomerular Filtration Rate Decreased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Weight Decreased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Procedural Pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Angina Pectoris			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Headache			
subjects affected / exposed	2 / 10 (20.00%)	3 / 10 (30.00%)	1 / 10 (10.00%)
occurrences (all)	2	3	1
Sciatica			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Neutropenia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Eye Pruritus			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal Discomfort			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Abdominal Pain Lower			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Abdominal Pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Abdominal Pain Upper			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Gastritis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1

Gastrointestinal Sounds Abnormal			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Lip Blister			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Hypoaesthesia Oral			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	4	0	1
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Alopecia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Rash Macular			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rash Maculo-Papular			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Renal Tubular Disorder			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			

Back Pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Arthralgia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Groin Pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal Chest Pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal Pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	0 / 10 (0.00%)
occurrences (all)	1	2	0
Neck Pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pain in Extremity			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Covid-19			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	2 / 10 (20.00%)
occurrences (all)	1	2	2
Influenza			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Nasopharyngitis			

subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Root Canal Infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Tinea Versicolour			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Urinary Tract Infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	2	0

Non-serious adverse events	FU Phase: Panel 1	FU Phase: Panel 3	OL Phase: Panel 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 10 (50.00%)	3 / 4 (75.00%)	3 / 4 (75.00%)
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 10 (0.00%)	2 / 4 (50.00%)	1 / 4 (25.00%)
occurrences (all)	0	2	1
Influenza Like Illness			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Chills			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injection Site Bruising			

subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injection Site Reaction			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injection Site Pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injection Site Erythema			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Vaginal Haemorrhage			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nasal Congestion			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Oropharyngeal Pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Productive Cough			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			

Mood Swings			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Depressed Mood			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Amylase Increased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Body Temperature Increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Low Density Lipoprotein Increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Glomerular Filtration Rate Decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Weight Decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Procedural Pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			

Angina Pectoris			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	2 / 10 (20.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	2	1	0
Sciatica			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	1 / 4 (25.00%)
occurrences (all)	0	2	1
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eye Pruritus			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal Discomfort			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Abdominal Pain Lower			

subjects affected / exposed	2 / 10 (20.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Abdominal Pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Abdominal Pain Upper			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Gastritis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal Sounds Abnormal			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lip Blister			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia Oral			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0

Pruritus			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rash Macular			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Rash Maculo-Papular			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Renal Tubular Disorder			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Groin Pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal Chest Pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal Pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Neck Pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Pain in Extremity			

subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Covid-19			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Influenza			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Root Canal Infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Tinea Versicolour			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Urinary Tract Infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 October 2021	The primary reasons for this amendment was to remove JNJ-6379 as study intervention, to add a new nucleos(t)ide analog (NA) re-treatment criterion for subjects who discontinued NA treatment during follow-up, and to include more frequent monitoring for subjects who discontinued NA treatment during follow-up.
25 November 2021	The primary purpose of this protocol amendmentwas to update the criteria for post-treatment monitoring and for nucleos(t)ide analog (NA) re-treatment for subjects who discontinued NA treatment at Week 48.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported