Clinical trial results:
A Randomized, Double-blind, Placebo-controlled Phase 2b Study to Evaluate Efficacy, Pharmacokinetics, and Safety of 48-week Study Intervention With JNJ-73763989+JNJ-56136379+Nucleos(t)ide Analog (NA) Regimen Compared to NA Alone in e Antigen-negative Virologically Suppressed Participants With Chronic Hepatitis B Virus Infection

Summary

EudraCT number	2019-002674-31
Trial protocol	BE DE FR PL ES IT
Global end of trial date	09 June 2022

Results information

Result version number	v1 (current)
This version publication date	24 June 2023
First version publication date	24 June 2023

Trial information

Trial identification

Sponsor protocol code	73763989PAHPB2002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04129554
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Sciences Ireland Unlimited Company
Sponsor organisation address	Ringaskiddy, Co. Cork, Barnahely, Ireland, P43 E773
Public contact	Clinical Registry Group, Janssen Sciences Ireland Unlimited Company, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Sciences Ireland Unlimited Company, 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	09 June 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 June 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study was to evaluate the efficacy of 48-week study intervention with JNJ-73763989+JNJ-56136379+nucleos(t)ide analog (NA) regimen compared to NA alone assessed by hepatitis B surface antigen (HBsAg) levels.

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 Practice and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 November 2019
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: 9
Country: Number of subjects enrolled	Germany: 12
Country: Number of subjects enrolled	Spain: 25
Country: Number of subjects enrolled	France: 21
Country: Number of subjects enrolled	United Kingdom: 18
Country: Number of subjects enrolled	Italy: 22
Country: Number of subjects enrolled	Poland: 23
Worldwide total number of subjects	130
EEA total number of subjects	112

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)	127
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 130 subjects were enrolled and randomised in the study, out of which 121 subjects completed the study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Nucleos(t)ide analog (NA)

Arm description:

Subjects received matching placebo for JNJ-73763989 by subcutaneous injection once every 4 weeks, along with matching placebo for JNJ-56136379 once daily and NA treatment (either entecavir [ETV], tenofovir disoproxil fumarate [TDF] or tenofovir alafenamide [TAF]) once daily up to 48 weeks.

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

Dosage and administration details:

Subjects received matching placebo for JNJ-73763989 once every 4 weeks up to 48 weeks.

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

Dosage and administration details:

Subjects received matching placebo for JNJ-56136379 once daily up to 48 weeks

Investigational medicinal product name	Entecavir (ETV) monohydrate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received ETV monohydrate 0.5 milligrams (mg) once daily up to 48 weeks as NA treatment.

Investigational medicinal product name	Tenofovir disoproxil fumarate (TDF)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received TDF 300 mg once daily up to 48 weeks as NA treatment.

Investigational medicinal product name	Tenofovir alafenamide (TAF)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received TAF 25 mg once daily up to 48 weeks as NA treatment.

Arm title	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA

Arm description:

Subjects received JNJ-73763989 200 mg subcutaneously, once every 4 weeks, along with JNJ-56136379 250 mg tablet, once daily and NA treatment (either ETV, TDF, or TAF) once daily up to 48 weeks.

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

Dosage and administration details:

Subjects received JNJ-73763989 200 mg once every 4 weeks up to 48 weeks.

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 once daily up to 48 weeks

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

Dosage and administration details:

Subjects received ETV 0.5 mg once daily up to 48 weeks as NA treatment.

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

Dosage and administration details:

Subjects received TDF 300 mg once daily up to 48 weeks as NA treatment.

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

Dosage and administration details:

Subjects received TAF 25 mg once daily up to 48 weeks as NA treatment.

Number of subjects in period 1	Nucleos(t)ide analog (NA)	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250
Started	45	85
Completed	40	81
Not completed	5	4
Consent withdrawn by subject	3	4
Unspecified	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Nucleos(t)ide analog (NA)
Reporting group description:	
Subjects received matching placebo for JNJ-73763989 by subcutaneous injection once every 4 weeks, along with matching placebo for JNJ-56136379 once daily and NA treatment (either entecavir [ETV], tenofovir disoproxil fumarate [TDF] or tenofovir alafenamide [TAF]) once daily up to 48 weeks.	
Reporting group title	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA
Reporting group description:	
Subjects received JNJ-73763989 200 mg subcutaneously, once every 4 weeks, along with JNJ-56136379 250 mg tablet, once daily and NA treatment (either ETV, TDF, or TAF) once daily up to 48 weeks.	

Reporting group values	Nucleos(t)ide analog (NA)	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250	Total
Number of subjects	45	85	130
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	44	83	127
From 65 to 84 years	1	2	3
85 years and over	0	0	0
Title for AgeContinuous Units: years			
arithmetic mean	47.4	45.3	
standard deviation	± 10.55	± 10.1	-
Title for Gender Units: subjects			
Female	16	27	43
Male	29	58	87

End points

End points reporting groups

Reporting group title	Nucleos(t)ide analog (NA)
Reporting group description:	
Subjects received matching placebo for JNJ-73763989 by subcutaneous injection once every 4 weeks, along with matching placebo for JNJ-56136379 once daily and NA treatment (either entecavir [ETV], tenofovir disoproxil fumarate [TDF] or tenofovir alafenamide [TAF]) once daily up to 48 weeks.	
Reporting group title	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA
Reporting group description:	
Subjects received JNJ-73763989 200 mg subcutaneously, once every 4 weeks, along with JNJ-56136379 250 mg tablet, once daily and NA treatment (either ETV, TDF, or TAF) once daily up to 48 weeks.	

Primary: Percentage of Subjects with Hepatitis B Surface Antigen (HBsAg) Seroclearance Without Restarting NA Treatment at Week 72

End point title	Percentage of Subjects with Hepatitis B Surface Antigen (HBsAg) Seroclearance Without Restarting NA Treatment at Week 72[1]
End point description:	
Percentage of subjects with HBsAg seroclearance at week 72 (24 weeks after completion of all study interventions at Week 48) without restarting NA treatment was reported. Seroclearance at Week 72 of the treatment defined as a confirmed loss of HBsAg at Week 72. Loss is defined as a baseline HBsAg with a repeat reactive, confirmed or positive result and a post-baseline assessment with a negative result. This outcome measure was planned to be analyzed at specified timepoint only. Modified intent-to-treat (mITT) was defined as all subjects who were randomized in the study and received at least one dose of study intervention excluding those subjects impacted by the pandemic. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this end point.	
End point type	Primary
End point timeframe:	
Week 72	

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 planned for this primary endpoint.

End point values	Nucleos(t)ide analog (NA)	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	79		
Units: Percentage of subjects				
number (not applicable)	0.0	0.0		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Treatment Emergent Serious Adverse Events (SAEs)

End point title	Percentage of Subjects with Treatment Emergent Serious Adverse Events (SAEs)[2]

End point description:

An AE was any untoward medical occurrence in a clinical study subject who was administered a pharmaceutical (investigational or non investigational) product. An AE does not necessarily have a causal relationship with the pharmaceutical/biological agent under study. TEAE was defined as the AEs occurring after first administration of study intervention (or worsened since then). SAEs included any untoward medical occurrence that resulted in death, were life-threatening, required hospitalization or prolongation of existing hospitalization, resulted in disability/incapacity or was a congenital anomaly/birth defect in the off spring of a study subject. Safety analysis set included all randomised subjects who received at least 1 dose of study drug. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this end point and 'n' (number evaluable) signifies number of subjects analysed at each specified timepoints.

End point type	Primary

End point timeframe:

Up to Week 102

Notes:

[2] - 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 planned for this primary endpoint.

End point values	Nucleos(t)ide analog (NA)	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	85		
Units: Percentage of subjects				
number (not applicable)	8.9	3.5		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Treatment Emergent Adverse Events (TEAEs)

End point title	Percentage of Subjects with Treatment Emergent Adverse Events (TEAEs)[3]

End point description:

An adverse event (AE) was any untoward medical occurrence in a clinical study subject who was administered a pharmaceutical (investigational or non investigational) product. An AE does not necessarily have a causal relationship with the pharmaceutical/biological agent under study. TEAE was defined as the AEs occurring after first administration of study intervention (or worsened since then). Safety assessments included regular monitoring of hematology, blood chemistry, blood coagulation, urine analysis, urine chemistry, renal biomarkers; periodic measurement of vital signs and electrocardiograms (ECGs); and performance of physical examinations. Safety analysis set included all randomised subjects who received at least 1 dose of study drug. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint and 'n' (number evaluable) signifies number of subjects analysed at each specified timepoints.

End point type	Primary

End point timeframe:

Up to Week 102

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 planned for this primary endpoint.

End point values	Nucleos(t)ide analog (NA)	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	85		
Units: Percentage of subjects				
number (not applicable)	80.0	85.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with HBsAg Seroclearance at Week 48

End point title	Percentage of Subjects with HBsAg Seroclearance at Week 48

End point description:

Percentage of subjects with hepatitis B surface antigen (HBsAg) seroclearance at Week 48 were reported. mITT was defined as all subjects who were randomized in the study and received at least one dose of study intervention excluding those subjects impacted by the pandemic. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 48

End point values	Nucleos(t)ide analog (NA)	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	84		
Units: Percentage of subjects				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Hepatitis B virus (HBV) Deoxyribonucleic Acid (DNA) Less Than (<) Lower Limit of Quantification (LLOQ)

End point title	Percentage of Subjects with Hepatitis B virus (HBV) Deoxyribonucleic Acid (DNA) Less Than (<) Lower Limit of Quantification (LLOQ)

End point description:

Percentage of subjects with HBV DNA <LLOQ (20 international units per millilitres [IU/mL]) at week 48 was reported. mITT was defined as all subjects who were randomized in the study and received at least one dose of study intervention excluding those subjects impacted by the pandemic. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 48

End point values	Nucleos(t)ide analog (NA)	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	84		
Units: Percentage of subjects				
number (not applicable)	100	97.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with (Sustained) Reduction, Suppression, and/or Seroclearance

End point title	Percentage of Subjects with (Sustained) Reduction, Suppression, and/or Seroclearance

End point description:

Percentage of subjects with (sustained) reduction, suppression, and/or seroclearance considering single and multiple markers (such as hepatitis B surface antigen [HBsAg] and HBV DNA) off-treatment were reported. mITT was defined as all subjects who were randomized in the study and received at least one dose of study intervention excluding those subjects impacted by the pandemic. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Up to Week 96

End point values	Nucleos(t)ide analog (NA)	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	84		

Units: Percentage of subjects				
number (not applicable)				
HBsAg>=LLOQ HBVDNA<2000 IU/mL	3.6	23.9		
HBsAg>=LLOQ and HBV DNA LLOQ <= and <2000 IU/mL	64.3	64.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with HBsAg Seroclearance at Week 96 (48 Weeks After Stopping All Study Interventions at Week 48 Without Restarting NA Treatment)

End point title	Percentage of Subjects with HBsAg Seroclearance at Week 96 (48 Weeks After Stopping All Study Interventions at Week 48 Without Restarting NA Treatment)

End point description:

Percentage of subjects with HBsAg seroclearance at Week 96 (48 weeks after stopping all study interventions at Week 48 without restarting NA treatment) was reported. mITT was defined as all subjects who were randomized in the study and received at least one dose of study intervention excluding those subjects impacted by the pandemic. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 96

End point values	Nucleos(t)ide analog (NA)	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	84		
Units: Percentage of subjects				
number (not applicable)	0.0	0.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with HBsAg Seroconversion at Week 96

End point title	Percentage of Subjects with HBsAg Seroconversion at Week 96

End point description:

HBsAg seroconversion was defined as HBsAg seroclearance together with appearance of anti-hepatitis B surface (HBs) or anti-hepatitis e (HBe) antibodies, respectively. Percentage of subjects with HBsAg seroconversion were reported. mITT was defined as all subjects who were randomized in the study and received at least one dose of study intervention excluding those subjects impacted by the pandemic. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint.

End point type	Secondary
End point timeframe: Week 96	

End point values	Nucleos(t)ide analog (NA)	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	84		
Units: Percentage of subjects				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in HBsAg at Weeks 48, 72 and 96

End point title	Change from Baseline in HBsAg at Weeks 48, 72 and 96
End point description: Change from baseline in HBsAg was reported. mITT was defined as all subjects who were randomized in the study and received at least one dose of study intervention excluding those subjects impacted by the pandemic. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint and 'n' (number evaluable) signifies number of subjects analysed at each specified timepoints.	
End point type	Secondary
End point timeframe: Baseline, Weeks 48, 72, and 96	

End point values	Nucleos(t)ide analog (NA)	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	81		
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Week 48 (n=41, 76)	-0.06 (± 0.082)	-1.89 (± 0.522)		
Week 72 (n=39, 79)	-0.25 (± 0.563)	-1.76 (± 0.658)		
Week 96 (n=40, 81)	-0.49 (± 0.783)	-1.46 (± 0.661)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in HBV DNA at Weeks 48, 72 and 96

End point title	Change from Baseline in HBV DNA at Weeks 48, 72 and 96

End point description:

Change from baseline in HBV DNA were reported. mITT was defined as all subjects who were randomized in the study and received at least one dose of study intervention excluding those subjects impacted by the pandemic. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this end point.

End point type	Secondary

End point timeframe:

Baseline, Weeks 48, 72, and 96

End point values	Nucleos(t)ide analog (NA)	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	78		
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Week 48 (n=39, 74)	0.03 (± 0.123)	-0.06 (± 0.221)		
Week 72 (n=36, 76)	0.30 (± 0.736)	-0.02 (± 0.118)		
Week 96 (n=38, 78)	0.09 (± 0.319)	0.00 (± 0.153)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with HBsAg Levels Greater Than (>) 1 log10 IU/mL Decline From Baseline

End point title	Percentage of Subjects with HBsAg Levels Greater Than (>) 1 log10 IU/mL Decline From Baseline

End point description:

Percentage of subjects with HBsAg Levels >1 log10 IU/mL decline from baseline were reported. mITT was defined as all subjects who were randomized in the study and received at least one dose of study intervention excluding those subjects impacted by the pandemic. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 96

End point values	Nucleos(t)ide analog (NA)	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	81		
Units: Percentage of subjects				
number (not applicable)	12.5	81.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Achieve First HBsAg Seroclearance

End point title	Time to Achieve First HBsAg Seroclearance

End point description:

Time to achieve first HBsAg seroclearance was defined as the number of days between the date of first study treatment intake and the date of the first occurrence of HBsAg seroclearance. mITT was defined as all subjects who were randomized in the study and received at least one dose of study intervention excluding those subjects impacted by the pandemic. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint. Here, '99999' indicated that since there were only less number of events reported therefore, the median survival time was not estimable.

End point type	Secondary

End point timeframe:

Up to Week 96

End point values	Nucleos(t)ide analog (NA)	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	83		
Units: Days				
median (full range (min-max))	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with HBsAg Levels Less Than (<) 100 IU/mL at Weeks 48, 72, and 96

End point title	Percentage of Subjects with HBsAg Levels Less Than (<) 100 IU/mL at Weeks 48, 72, and 96

End point description:

Percentage of subjects with HBsAg Levels <100 IU/mL at different timepoints were reported. mITT was defined as all subjects who were randomized in the study and received at least one dose of study intervention excluding those subjects impacted by the pandemic. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Weeks 48, 72, and 96

End point values	Nucleos(t)ide analog (NA)	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	84		
Units: Percentage of subjects				
number (not applicable)				
Week 48 (n=41, 76)	2.4	71.1		
Week 72 (n=39, 79)	10.3	67.1		
Week 96 (n=40, 81)	15.0	46.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with HBV DNA Levels Less Than (<) LLOQ

End point title	Percentage of Subjects with HBV DNA Levels Less Than (<) LLOQ

End point description:

Percentage of Subjects with HBV DNA levels <LLOQ were reported. mITT was defined as all subjects who were randomized in the study and received at least one dose of study intervention excluding those subjects impacted by the pandemic. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 96

End point values	Nucleos(t)ide analog (NA)	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	71		
Units: Percentage of subjects				
number (not applicable)	3.6	23.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Flares

End point title	Percentage of Subjects with Flares

End point description:

Percentage of subjects with flares (virologic, biochemical and clinical flares) were reported. Biochemical flare was defined as confirmed alanine transaminase flare and/or aspartate aminotransferase flare >=3*upper limit of normal and >=3*nadir. Virologic flare was defined per Derivation 1 (2 consecutive visits) HBV DNA >peak threshold in subjects who were off-treatment and had HBV DNA <LLOQ at the last observed time point on all study interventions and per Derivation 2 (2 consecutive visits) HBV DNA >peak threshold in subjects who were off-treatment and had HBVDNA >=LLOQ at the last observed time point on all study interventions. Clinical flare was defined as subjects with both virologic and biochemical flare. mITT was defined as all subjects who were randomized in the study and received at least one dose of study intervention excluding those subjects impacted by the pandemic. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 96

End point values	Nucleos(t)ide analog (NA)	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	84		
Units: Percentage of subjects				
number (not applicable)				
Virologic Flare (HBV DNA > 200 - =<2000 IU/mL)	25.0	38.7		
Virologic Flare (HBV DNA>2000 - =< 20000 IU/mL)	30.0	24.0		
Virologic Flare (HBV DNA >20000 - =<100000 IU/mL)	10.0	8.0		
Virologic Flare (HBV DNA >100000 IU/mL)	27.5	2.7		
Alanine Transaminase Flare	19.5	3.9		
Aspartate Aminotransferase Flare	14.6	1.3		
Biochemical Flare	19.5	3.9		

Clinical Flare: HBV DNA > 200 - =<2000IU/mL	0.0	0.0		
Clinical Flare: HBV DNA > 2000 - =<20000IU/mL	0.0	1.3		
Clinical Flare: HBV DNA > 20000 - =<100000IU/mL	0.0	1.3		
Clinical Flare: HBV DNA > 100000 IU/mL	27.5	1.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Virologic Breakthrough

End point title	Percentage of Subjects with Virologic Breakthrough

End point description:

Percentage of subjects with virologic breakthrough defined as confirmed on-treatment HBV DNA increase by greater than (>) 1 log10 IU/mL from nadir level or confirmed on treatment level >200 IU/mL in subjects who had HBV DNA level below <LLOQ of the HBV DNA assay were reported. mITT was defined as all subjects who were randomized in the study and received at least one dose of study intervention excluding those subjects impacted by the pandemic. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 48

End point values	Nucleos(t)ide analog (NA)	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	84		
Units: Percentage of subjects				
number (not applicable)	0.0	0.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Requiring NA Re-Treatment During Follow-up

End point title	Percentage of Subjects Requiring NA Re-Treatment During Follow-up

End point description:

Percentage of subjects requiring NA re-treatment during follow-up were reported. mITT was defined as all subjects who were randomized in the study and received at least one dose of study intervention excluding those subjects impacted by the pandemic. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint.

End point type	Secondary
End point timeframe: Week 96	

End point values	Nucleos(t)ide analog (NA)	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	84		
Units: Percentage of subjects				
number (not applicable)	26.8	9.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation Coefficient Between On-treatment HBsAg Change from Baseline with On-treatment HBV Blood Markers and Baseline Characteristics

End point title	Correlation Coefficient Between On-treatment HBsAg Change from Baseline with On-treatment HBV Blood Markers and Baseline Characteristics

End point description:

Correlation coefficient between on-treatment HBsAg change from baseline with on-treatment HBV blood markers and baseline characteristics were reported. HBsAg change from baseline at FU Week 24 were analysed against age, baseline NA treatment duration, HBsAg value at baseline, HBsAg change from baseline at Week 24, and HBsAg change from baseline at Week 48. Here, baseline is specified as 'bs', duration as 'du', change as 'chn' and week 'wk'. mITT was defined as all subjects who were randomized in the study and received at least one dose of study intervention excluding those subjects impacted by the pandemic. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this outcome measure.

End point type	Secondary
End point timeframe: Baseline to Week 96	

End point values	Nucleos(t)ide analog (NA)	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	84		
Units: Ratio				
number (not applicable)				
HBsAg chn from bs vs Age (n=39, 79)	0.1746	0.2860		

HBsAg chn from bs vs bs NA treatment du (n=39,78)	0.4324	0.2381		
HBsAg chn from bs vs HBsAg value at bs (n=39, 79)	-0.5923	-0.9970		
HBsAg chn from bs at FU Wk 48 vs Wk 24(n=39, 74)	0.7120	0.9983		
HBsAg chn from bs at FU Wk 48 vs Wk 48 (n=39, 74)	0.8065	0.9982		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Analyte Concentration (Cmax) of Dose Normalized to 1 mg (Cmax[Dose Normalised]) of JNJ-73763976

End point title	Maximum Observed Analyte Concentration (Cmax) of Dose Normalized to 1 mg (Cmax[Dose Normalised]) of JNJ-73763976[4]

End point description:

Cmax(Dose Normalised) was defined as the maximum observed analyte concentration of JNJ-73763976 dose normalized to 1 mg. PK analysis set included subjects who had received at least 1 dose of any of the study interventions and had at least 1 valid blood sample drawn for PK analysis. Here, 'N' (number analysed) signifies number of subjects analysed for this end point. NA was TDF.

End point type	Secondary

End point timeframe:

Up to Day 337

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint was planned to be analysed for specified arms only.

End point values	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: ng/mL/mg				
arithmetic mean (standard deviation)	8.34 (± 5.37)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Analyte Concentration Versus Time Curve From Time 0 to 24 h (AUC[0-24h]) of JNJ-73763976

End point title	Area Under the Analyte Concentration Versus Time Curve From Time 0 to 24 h (AUC[0-24h]) of JNJ-73763976[5]

End point description:

AUC(0-24h) was defined as the area under the analyte concentration versus time curve from time 0 to

24 h of JNJ-73763976. PK analysis set included subjects who had received at least 1 dose of any of the study interventions and had at least 1 valid blood sample drawn for PK analysis. Here, 'N' (number analysed) signifies number of subjects analysed for this end point. NA was TDF.

End point type	Secondary

End point timeframe:

24 hours postdose

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed for specified arms only.

End point values	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: nanogram*hour/millilitre (ng*h/mL)				
arithmetic mean (standard deviation)	17833 (± 9670)			

Statistical analyses

No statistical analyses for this end point

Secondary: Observed Concentration at 24 h Postdose (C[24h]) of JNJ-73763976

End point title	Observed Concentration at 24 h Postdose (C[24h]) of JNJ-73763976[6]

End point description:

C(24h) was defined as the observed concentration at 24 h postdose of JNJ-73763976. PK analysis set included subjects who had received at least 1 dose of any of the study interventions and had at least 1 valid blood sample drawn for PK analysis. Here, 'N' (number analysed) signifies number of subjects analysed for this end point. NA was TDF.

End point type	Secondary

End point timeframe:

24 hours postdose

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed for specified arms only.

End point values	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: ng/mL				
arithmetic mean (standard deviation)	275 (± 161)			

Statistical analyses

No statistical analyses for this end point

Secondary: Observed Concentration at Predose (C[predose]) of JNJ-73763976

End point title	Observed Concentration at Predose (C[predose]) of JNJ-73763976[7]

End point description:

C(predose) was defined as the observed concentration at predose of JNJ-73763976. Pharmacokinetic (PK) analysis set was defined as subjects who had received at least 1 dose of any of the study interventions and had at least 1 valid blood sample drawn for PK analysis. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint. NA was tenofovir disoproxil fumarate (TDF). Here, '99999'' indicated that data was below quantification limit (<2.1 ng/mL).

End point type	Secondary

End point timeframe:

Predose

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed for specified arms only.

End point values	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: nanogram/millilitre (ng/mL)				
arithmetic mean (standard deviation)	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Analyte Concentration (Cmax) of JNJ-73763976

End point title	Maximum Observed Analyte Concentration (Cmax) of JNJ-73763976[8]

End point description:

Cmax was defined as the maximum concentration of JNJ-73763976. PK analysis set included subjects who had received at least 1 dose of any of the study interventions and had at least 1 valid blood sample drawn for PK analysis. NA was TDF. Here, 'N' (number analysed) signifies number of subjects analysed for this end point.

End point type	Secondary

End point timeframe:

Up to Day 337

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed for specified arms only.

End point values	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: ng/mL				
arithmetic mean (standard deviation)	1111 (± 716)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach the Maximum Observed Plasma Concentration (tmax) of JNJ-73763976

End point title	Time to Reach the Maximum Observed Plasma Concentration (tmax) of JNJ-73763976[9]

End point description:

tmax was defined as the time to reach the maximum observed plasma concentration of JNJ-73763976. PK analysis set included subjects who had received at least 1 dose of any of the study interventions and had at least 1 valid blood sample drawn for PK analysis. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this outcome measure. NA was TDF.

End point type	Secondary

End point timeframe:

Up to Day 337

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed for specified arms only.

End point values	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: Hour				
median (full range (min-max))	6.00 (1.00 to 10.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: Observed Concentration at Predose (C[predose]) of JNJ-73763924

End point title	Observed Concentration at Predose (C[predose]) of JNJ-73763924[10]

End point description:

C(predose) was defined as the observed concentration at predose of JNJ-73763924. PK analysis set was defined as subjects who had received at least 1 dose of any of the study interventions and had at least 1 valid blood sample drawn for PK analysis. Here, 'N' (number analysed) signifies number of subjects analysed at each specified endpoint. NA was tenofovir disoproxil fumarate (TDF). Here, '99999'' indicates that data was below quantification limit (<2.1 ng/mL).

End point type	Secondary

End point timeframe:

Predose

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed for specified arms only.

End point values	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: ng/mL				
arithmetic mean (standard deviation)	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach the Maximum Observed Plasma Concentration (tmax) of JNJ-73763924

End point title	Time to Reach the Maximum Observed Plasma Concentration (tmax) of JNJ-73763924[11]

End point description:

tmax was defined as the time to reach the maximum observed plasma concentration of JNJ-73763924. PK analysis set included subjects who had received at least 1 dose of any of the study interventions and had at least 1 valid blood sampl6e drawn for PK analysis. Here, 'N' (number analysed) signifies number of subjects analysed for this end point. NA was TDF.

End point type	Secondary

End point timeframe:

Up to Day 337

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed for specified arms only.

End point values	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: Hour				
median (full range (min-max))	5.07 (1.00 to 8.03)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Analyte Concentration (Cmax) of JNJ-73763924

End point title	Maximum Observed Analyte Concentration (Cmax) of JNJ-73763924[12]

End point description:

Cmax was defined as the maximum concentration of JNJ-73763924. PK analysis set included subjects who had received at least 1 dose of any of the study interventions and had at least 1 valid blood sample drawn for PK analysis. NA was TDF. Here, 'N' (number analysed) signifies number of subjects analysed for this end point.

End point type	Secondary

End point timeframe:

Up to Day 337

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed for specified arms only.

End point values	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: ng/mL				
arithmetic mean (standard deviation)	222 (± 142)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Analyte Concentration (Cmax) of Dose Normalized to 1 mg (Cmax[Dose Normalised]) of JNJ-73763924

End point title	Maximum Observed Analyte Concentration (Cmax) of Dose Normalized to 1 mg (Cmax[Dose Normalised]) of JNJ-

	73763924[13]

End point description:

Cmax(Dose Normalised) was defined as the maximum observed analyte concentration of JNJ-73763924 dose normalized to 1 mg. PK analysis set included subjects who had received at least 1 dose of any of the study interventions and had at least 1 valid blood sample drawn for PK analysis. Here, 'N' (number analysed) signifies number of subjects analysed for this end point. NA was TDF.

End point type	Secondary

End point timeframe:

Up to Day 337

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed for specified arms only.

End point values	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: nanogram/milliliter/milligram (ng/mL/mg)				
arithmetic mean (standard deviation)	3.33 (± 2.14)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Analyte Concentration Versus Time Curve From Time 0 to 24 h (AUC[0-24h]) of JNJ-73763924

End point title	Area Under the Analyte Concentration Versus Time Curve From Time 0 to 24 h (AUC[0-24h]) of JNJ-73763924[14]

End point description:

AUC(0-24h) was defined as the area under the analyte concentration versus time curve from time 0 to 24 h of JNJ-73763924. PK analysis set included subjects who had received at least 1 dose of any of the study interventions and had at least 1 valid blood sample drawn for PK analysis. Here, 'N' (number analysed) signifies number of subjects analysed for this end point. NA was TDF.

End point type	Secondary

End point timeframe:

24 hour postdose

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed for specified arms only.

End point values	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: ng*h/mL				
arithmetic mean (standard deviation)	3386 (± 1930)			

Statistical analyses

No statistical analyses for this end point

Secondary: Observed Concentration at 24 h Postdose (C[24h]) of JNJ-73763924

End point title	Observed Concentration at 24 h Postdose (C[24h]) of JNJ-73763924[15]

End point description:

C(24h) was defined as the observed concentration at 24 h postdose of JNJ-73763924. PK analysis set included subjects who had received at least 1 dose of any of the study interventions and had at least 1 valid blood sample drawn for PK analysis. Here, 'N' (number analysed) signifies number of subjects analysed for this end point. NA was TDF.

End point type	Secondary

End point timeframe:

24 hour postdose

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: This endpoint was planned to be analysed for specified arms only.

End point values	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: ng/mL				
arithmetic mean (standard deviation)	35.0 (± 25.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Analyte Concentration Versus Time Curve From Time 0 to 24 h of Dose Normalized to 1 mg (AUC[0-24h], Dose Normalised) of JNJ-73763976

End point title	Area Under the Analyte Concentration Versus Time Curve From Time 0 to 24 h of Dose Normalized to 1 mg (AUC[0-24h], Dose Normalised) of JNJ-73763976[16]

End point description:

AUC([0-24h], Dose Normalised) was defined as the area under the analyte concentration versus time curve from time 0 to 24 h of JNJ-73763976 dose normalized to 1 mg. PK analysis set included subjects who had received at least 1 dose of any of the study interventions and had at least 1 valid blood sample drawn for PK analysis. Here, 'N' (number analysed) signifies number of subjects analysed for this end point. NA was TDF.

End point type	Secondary

End point timeframe:

Up to Day 337

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: This endpoint was planned to be analysed for specified arms only.

End point values	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: ng*h/mL/mg				
arithmetic mean (standard deviation)	134 (± 72.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach the Maximum Observed Plasma Concentration (tmax) of JNJ-56136379

End point title	Time to Reach the Maximum Observed Plasma Concentration (tmax) of JNJ-56136379[17]

End point description:

tmax was defined as the time to reach the maximum observed plasma concentration of JNJ-56136379. PK analysis set included subjects who had received at least 1 dose of any of the study interventions and had at least 1 valid blood sample drawn for PK analysis. Here, 'N' (number analysed) signifies number of subjects analysed for this end point. NA was TDF.

End point type	Secondary

End point timeframe:

Up to Day 337

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: This endpoint was planned to be analysed for specified arms only.

End point values	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA			
Subject group type	Reporting group			
Number of subjects analysed	12			

Units: Hour				
median (full range (min-max))	4.00 (0.0 to 24.17)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Analyte Concentration Versus Time Curve During a Dosing Interval at Steady State (AUCtau) of JNJ-56136379

End point title	Area Under the Analyte Concentration Versus Time Curve During a Dosing Interval at Steady State (AUCtau) of JNJ-56136379[18]

End point description:

AUCtau was defined as the area under the analyte concentration versus time curve during a dosing interval at steady state of JNJ-56136379. PK analysis set included subjects who have received at least 1 dose of any of the study interventions and have at least 1 valid blood sample drawn for PK analysis. Here, 'N' (number analysed) signifies number of subjects analysed for this end point. NA was TDF.

End point type	Secondary

End point timeframe:

Up to Day 337

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: This endpoint was planned to be analysed for specified arms only.

End point values	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: ng*h/mL				
arithmetic mean (standard deviation)	282458 (± 79118)			

Statistical analyses

No statistical analyses for this end point

Secondary: Observed or Predicted Concentration at the End of a Dosing Interval (Ctau) of JNJ-56136379

End point title	Observed or Predicted Concentration at the End of a Dosing Interval (Ctau) of JNJ-56136379[19]

End point description:

Ctau was defined as the observed or predicted concentration at the end of a dosing interval of JNJ-56136379. PK analysis set included subjects who had received at least 1 dose of any of the study interventions and had at least 1 valid blood sample drawn for PK analysis. Here, 'N' (number analysed) signifies number of subjects analysed for this end point. NA was TDF.

End point type	Secondary

End point timeframe:

Up to Day 337

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: This endpoint was planned to be analysed for specified arms only.

End point values	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: ng/mL				
arithmetic mean (standard deviation)	12763 (± 4959)			

Statistical analyses

No statistical analyses for this end point

Secondary: Observed Concentration at Predose (C[predose]) of JNJ-56136379

End point title	Observed Concentration at Predose (C[predose]) of JNJ-56136379[20]

End point description:

C(predose) was defined as the observed concentration at predose of JNJ-56136379. PK analysis set was defined as subjects who had received at least 1 dose of any of the study interventions and had at least 1 valid blood sample drawn for PK analysis. Here, 'N' (number analysed) signifies number of subjects analysed at each specified end point. NA was tenofovir disoproxil fumarate (TDF).

End point type	Secondary

End point timeframe:

Predose

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed for specified arms only.

End point values	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: ng/mL				
arithmetic mean (standard deviation)	10812 (± 2430)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Analyte Concentration Versus Time Curve From Time 0 to 24 h of Dose Normalized to 1 mg (AUC[0-24h], Dose Normalised) of JNJ-73763924

End point title	Area Under the Analyte Concentration Versus Time Curve From Time 0 to 24 h of Dose Normalized to 1 mg (AUC[0-24h], Dose Normalised) of JNJ-73763924[21]

End point description:

AUC([0-24h], Dose Normalised) was defined as the area under the analyte concentration versus time curve from time 0 to 24 h of JNJ-73763924 dose normalized to 1 mg. PK analysis set included subjects who had received at least 1 dose of any of the study interventions and had at least 1 valid blood sample drawn for PK analysis. Here, 'N' (number analysed) signifies number of subjects analysed for this end point. NA was TDF.

End point type	Secondary

End point timeframe:

Up to Day 337

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed for specified arms only.

End point values	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: ng*h/mL/mg				
arithmetic mean (standard deviation)	50.8 (± 28.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Analyte Concentration (Cmax) of JNJ-56136379

End point title	Maximum Observed Analyte Concentration (Cmax) of JNJ-56136379[22]

End point description:

Cmax was defined as the maximum concentration of JNJ-56136379. PK analysis set included subjects who had received at least 1 dose of any of the study interventions and had at least 1 valid blood sample drawn for PK analysis. NA was TDF. Here, 'N' (number analysed) signifies number of subjects analysed for this end point.

End point type	Secondary

End point timeframe:

Up to Day 337

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was planned to be analysed for specified arms only.

End point values	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: ng/mL				
arithmetic mean (standard deviation)	14754 (± 4318)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Week 102 (including 6 weeks of screening)

Adverse event reporting additional description:

The safety analysis set included all subjects who received at least 1 dose of study drug.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250 mg)+NA

Reporting group description:

Subjects received JNJ-73763989 200 mg, subcutaneously, every 4 weeks, along with JNJ-56136379 250 mg, tablet, once daily and NA treatment (either ETV, TDF, or TAF) once daily up to 48 weeks.

Reporting group title	Nucleos(t)ide Analog (NA)

Reporting group description:

Subjects received matching placebo for JNJ-73763989 subcutaneously injection once every 4 weeks, with matching placebo for JNJ-56136379 once daily and NA treatment (either entecavir [ETV], tenofovir disoproxil fumarate [TDF] or tenofovir alafenamide [TAF]) once daily up to 48 weeks.

Serious adverse events	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250	Nucleos(t)ide Analog (NA)	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 85 (3.53%)	4 / 45 (8.89%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatic Cancer			
subjects affected / exposed	1 / 85 (1.18%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangiocarcinoma			
subjects affected / exposed	1 / 85 (1.18%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular Carcinoma			

subjects affected / exposed	0 / 85 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Radius Fracture			
subjects affected / exposed	0 / 85 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 85 (1.18%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 85 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Subacute Hepatic Failure			
subjects affected / exposed	0 / 85 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral Disc Disorder			
subjects affected / exposed	0 / 85 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Covid-19			
subjects affected / exposed	1 / 85 (1.18%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus Infection Reactivation			

subjects affected / exposed	1 / 85 (1.18%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis B Reactivation			
subjects affected / exposed	0 / 85 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	JNJ-73763989 (200 milligrams [mg])+JNJ-56136379 (250	Nucleos(t)ide Analog (NA)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	67 / 85 (78.82%)	34 / 45 (75.56%)	
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	6 / 85 (7.06%)	11 / 45 (24.44%)	
occurrences (all)	23	20	
Aspartate Aminotransferase Increased			
subjects affected / exposed	3 / 85 (3.53%)	4 / 45 (8.89%)	
occurrences (all)	9	10	
Hepatitis B DNA increased			
subjects affected / exposed	2 / 85 (2.35%)	3 / 45 (6.67%)	
occurrences (all)	2	3	
Glomerular Filtration Rate Decreased			
subjects affected / exposed	18 / 85 (21.18%)	4 / 45 (8.89%)	
occurrences (all)	30	5	
Vascular disorders			
Hypertension			
subjects affected / exposed	11 / 85 (12.94%)	3 / 45 (6.67%)	
occurrences (all)	12	3	
Nervous system disorders			
Headache			
subjects affected / exposed	19 / 85 (22.35%)	10 / 45 (22.22%)	
occurrences (all)	26	14	

General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	12 / 85 (14.12%)	4 / 45 (8.89%)	
occurrences (all)	15	4	
Fatigue			
subjects affected / exposed	11 / 85 (12.94%)	5 / 45 (11.11%)	
occurrences (all)	18	6	
Pyrexia			
subjects affected / exposed	8 / 85 (9.41%)	3 / 45 (6.67%)	
occurrences (all)	9	4	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	7 / 85 (8.24%)	3 / 45 (6.67%)	
occurrences (all)	7	4	
Diarrhoea			
subjects affected / exposed	3 / 85 (3.53%)	6 / 45 (13.33%)	
occurrences (all)	3	7	
Abdominal Pain			
subjects affected / exposed	2 / 85 (2.35%)	3 / 45 (6.67%)	
occurrences (all)	2	3	
Vomiting			
subjects affected / exposed	6 / 85 (7.06%)	1 / 45 (2.22%)	
occurrences (all)	9	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 85 (5.88%)	1 / 45 (2.22%)	
occurrences (all)	5	1	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 85 (1.18%)	4 / 45 (8.89%)	
occurrences (all)	1	4	
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	10 / 85 (11.76%)	5 / 45 (11.11%)	
occurrences (all)	12	7	
Arthralgia			

subjects affected / exposed	9 / 85 (10.59%)	9 / 45 (20.00%)	
occurrences (all)	12	13	
Muscle Spasms			
subjects affected / exposed	1 / 85 (1.18%)	3 / 45 (6.67%)	
occurrences (all)	1	4	
Myalgia			
subjects affected / exposed	6 / 85 (7.06%)	3 / 45 (6.67%)	
occurrences (all)	7	3	
Osteoarthritis			
subjects affected / exposed	0 / 85 (0.00%)	3 / 45 (6.67%)	
occurrences (all)	0	3	
Pain in Extremity			
subjects affected / exposed	9 / 85 (10.59%)	2 / 45 (4.44%)	
occurrences (all)	11	2	
Infections and infestations			
Covid-19			
subjects affected / exposed	17 / 85 (20.00%)	4 / 45 (8.89%)	
occurrences (all)	18	4	
Tooth Infection			
subjects affected / exposed	0 / 85 (0.00%)	4 / 45 (8.89%)	
occurrences (all)	0	5	
Nasopharyngitis			
subjects affected / exposed	10 / 85 (11.76%)	5 / 45 (11.11%)	
occurrences (all)	10	6	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 September 2019	The purpose of the amendment was to include the following changes: methods for handling of missing data, the exclusion criterion on allergies was broadened to also include placebo content, a reference to the prescribing information of ETV, TDF, and TAF was added, unblinding wording was updated to emphasize subject safety, and a more general recommendation to consider alternative concomitant medications or adjusted doses was provided.
20 January 2020	The purpose of the amendment was to include the following main changes: additional information for the management of hematologic abnormalities was provided and the preclinical section was updated to include the preliminary results from the 3-month combination toxicity study with JNJ-3989 and JNJ-6379.
30 September 2021	The purpose of the amendment was to include an additional NA re-treatment criterion as an urgent safety measure, after the report of a severe hepatitis B reactivation requiring liver transplantation following NA treatment discontinuation in a subject in the control arm.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported