Clinical trial results:
A Phase 2a, Randomized, Partially-blind, Placebo-controlled Study to Assess the Efficacy, Safety, and Pharmacokinetics of Treatment With Multiple Doses of JNJ-56136379 as Monotherapy and in Combination With a Nucleos(t)ide Analog in Subjects With Chronic Hepatitis B Virus Infection

Summary

EudraCT number	2017-001110-29
Trial protocol	GB BE DE ES PL IT
Global end of trial date	13 August 2020

Results information

Result version number	v1 (current)
This version publication date	29 August 2021
First version publication date	29 August 2021

Trial information

Trial identification

Sponsor protocol code	56136379HPB2001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03361956
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen-Cilag International NV
Sponsor organisation address	Archimedesweg 29, Leiden, Netherlands, 2333 CM
Public contact	Clinical Registry Group, Janssen-Cilag International NV, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen-Cilag International 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	13 August 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 August 2020
Global end of trial reached?	Yes
Global end of trial date	13 August 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to evaluate efficacy of 24 weeks of study treatment, in terms of changes in 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 Practices and applicable regulatory requirements. Safety evaluations were based upon the type, incidence, and severity of Treatment-emergent adverse events (TEAEs) reported throughout the study, and on changes in physical examination, vital sign measurements, clinical laboratory test results and electrocardiogram (ECG) results.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 February 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 11
Country: Number of subjects enrolled	Canada: 14
Country: Number of subjects enrolled	China: 18
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Spain: 12
Country: Number of subjects enrolled	France: 11
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	Hong Kong: 1
Country: Number of subjects enrolled	Italy: 10
Country: Number of subjects enrolled	Japan: 8
Country: Number of subjects enrolled	Korea, Republic of: 7
Country: Number of subjects enrolled	Malaysia: 8
Country: Number of subjects enrolled	Poland: 18
Country: Number of subjects enrolled	Russian Federation: 18
Country: Number of subjects enrolled	Thailand: 7
Country: Number of subjects enrolled	Turkey: 23
Country: Number of subjects enrolled	Taiwan: 32
Country: Number of subjects enrolled	Ukraine: 10

Country: Number of subjects enrolled	United States: 5
Worldwide total number of subjects	232
EEA total number of subjects	71

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)	230
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 232 subjects were enrolled and 211 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	JNJ-56136379- 75 mg (Open label)

Arm description:

Subjects currently not treated received 3*25 milligrams (mg) tablets of JNJ-56136379 once daily during the open label phase from Day 1 to Week 24.

Arm type	Experimental
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 75 mg of JNJ-56136379 administered as 3*25 mg of JNJ-56136379 tablets once daily orally during the open-label phase.

Arm title	Placebo (matching JNJ-6379 75mg) + Nucleos(t)ide analog (NA)

Arm description:

Subjects received 3 tablets of matching placebo plus 1 tablet of NA (0.5 mg entecavir [ETV] or 300 mg tenofovir disoproxil fumarate [TDF]) once daily from Day 1 to Week 24.

Arm type	Placebo
Investigational medicinal product name	Nucleos(t)ide analog (NA): ETV or TDF
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received a single tablet of 0.5 mg ETV or 300 mg TDF once daily orally.

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

Dosage and administration details:

Subjects received 3 tablets of matching placebo once daily orally.

Arm title	JNJ-56136379- 75 mg + NA

Arm description:

Subjects received 3*25 mg tablets of JNJ-56136379 plus 1 tablet of NA (0.5 mg ETV or 300 mg TDF) once daily from Day 1 to Week 24.

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

Dosage and administration details:

Subjects received a single tablet of 0.5 mg ETV or 300 mg TDF once daily orally.

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 75 mg of JNJ-56136379 administered as 3*25 mg of JNJ-56136379 tablets once daily orally.

Arm title	JNJ-56136379- 250 mg (Open label)

Arm description:

Subjects received 2*100 mg and 2*25 mg tablets of JNJ-56136379 once daily during the open-label phase from Day 1 to Week 24.

Arm type	Experimental
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 250 mg of JNJ-56136379 administered as 2*100 mg and 2*25 mg tablets of JNJ-56136379 once daily orally during the open label phase.

Arm title	Placebo (matching to JNJ-56136379 250 mg) + NA

Arm description:

Subjects received 2 tablets of matching placebo plus 1 tablet of NA (0.5 mg ETV or 300 mg TDF) once daily from Day 1 to Week 24.

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

Dosage and administration details:

Subjects received 4 tablets of matching placebo (2*100 mg and 2*25 mg) once daily orally.

Investigational medicinal product name	ETV or TDF
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received a single tablet of 0.5 mg ETV or 300 mg TDF once daily orally.

Arm title	JNJ-56136379- 250 mg + NA

Arm description:

Subjects received 2*100 mg and 2*25 mg tablets of JNJ-56136379 plus 1 tablet of NA (0.5 mg ETV or 300 mg TDF) once daily from Day 1 to Week 24.

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

Dosage and administration details:

Subjects received a single tablet of 0.5 mg ETV or 300 mg TDF once daily orally.

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 250 mg of JNJ-56136379 administered as 2*100 mg and 2*25 mg tablets of JNJ-56136379 once daily orally.

Number of subjects in period 1	JNJ-56136379- 75 mg (Open label)	Placebo (matching JNJ-6379 75mg) + Nucleos(t)ide analog (NA)	JNJ-56136379- 75 mg + NA
Started	28	21	66
Completed	24	21	61
Not completed	4	0	5
Physician decision	2	-	-
Adverse event, non-fatal	-	-	1
Other	-	-	-
Lost to follow-up	-	-	1
Withdrawal by subject	2	-	2
Lack of efficacy	-	-	1

Number of subjects in period 1	JNJ-56136379- 250 mg (Open label)	Placebo (matching to JNJ-56136379 250 mg) + NA	JNJ-56136379- 250 mg + NA
Started	32	22	63
Completed	28	19	58
Not completed	4	3	5
Physician decision	1	-	-
Adverse event, non-fatal	1	1	-
Other	1	-	-
Lost to follow-up	1	-	2
Withdrawal by subject	-	2	3
Lack of efficacy	-	-	-

Baseline characteristics

Reporting groups	
Reporting group title	JNJ-56136379- 75 mg (Open label)
Reporting group description:	
Subjects currently not treated received 3*25 milligrams (mg) tablets of JNJ-56136379 once daily during the open label phase from Day 1 to Week 24.	
Reporting group title	Placebo (matching JNJ-6379 75mg) + Nucleos(t)ide analog (NA)
Reporting group description:	
Subjects received 3 tablets of matching placebo plus 1 tablet of NA (0.5 mg entecavir [ETV] or 300 mg tenofovir disoproxil fumarate [TDF]) once daily from Day 1 to Week 24.	
Reporting group title	JNJ-56136379- 75 mg + NA
Reporting group description:	
Subjects received 3*25 mg tablets of JNJ-56136379 plus 1 tablet of NA (0.5 mg ETV or 300 mg TDF) once daily from Day 1 to Week 24.	
Reporting group title	JNJ-56136379- 250 mg (Open label)
Reporting group description:	
Subjects received 2*100 mg and 2*25 mg tablets of JNJ-56136379 once daily during the open-label phase from Day 1 to Week 24.	
Reporting group title	Placebo (matching to JNJ-56136379 250 mg) + NA
Reporting group description:	
Subjects received 2 tablets of matching placebo plus 1 tablet of NA (0.5 mg ETV or 300 mg TDF) once daily from Day 1 to Week 24.	
Reporting group title	JNJ-56136379- 250 mg + NA
Reporting group description:	
Subjects received 2*100 mg and 2*25 mg tablets of JNJ-56136379 plus 1 tablet of NA (0.5 mg ETV or 300 mg TDF) once daily from Day 1 to Week 24.	

Reporting group values	JNJ-56136379- 75 mg (Open label)	Placebo (matching JNJ-6379 75mg) + Nucleos(t)ide analog (NA)	JNJ-56136379- 75 mg + NA
Number of subjects	28	21	66
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	27	21	65
From 65 to 84 years	1	0	1
85 years and over	0	0	0
Title for AgeContinuous Units: years			
arithmetic mean	39.2	42.5	40.3
standard deviation	± 12.06	± 9.11	± 11.12
Title for Gender Units: subjects			
Female	9	8	20
Male	19	13	46

Reporting group values	JNJ-56136379- 250 mg (Open label)	Placebo (matching to JNJ-56136379 250 mg) + NA	JNJ-56136379- 250 mg + NA

Number of subjects	32	22	63
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	32	22	63
From 65 to 84 years	0	0	0
85 years and over	0	0	0
Title for AgeContinuous Units: years			
arithmetic mean	37.7	40.8	40.5
standard deviation	± 10.92	± 10.06	± 10.99
Title for Gender Units: subjects			
Female	14	6	13
Male	18	16	50

Reporting group values	Total		
Number of subjects	232		
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	230		
From 65 to 84 years	2		
85 years and over	0		
Title for AgeContinuous Units: years			
arithmetic mean			
standard deviation	-		
Title for Gender Units: subjects			
Female	70		
Male	162		

End points

End points reporting groups

Reporting group title	JNJ-56136379- 75 mg (Open label)
Reporting group description:	
Subjects currently not treated received 3*25 milligrams (mg) tablets of JNJ-56136379 once daily during the open label phase from Day 1 to Week 24.	
Reporting group title	Placebo (matching JNJ-6379 75mg) + Nucleos(t)ide analog (NA)
Reporting group description:	
Subjects received 3 tablets of matching placebo plus 1 tablet of NA (0.5 mg entecavir [ETV] or 300 mg tenofovir disoproxil fumarate [TDF]) once daily from Day 1 to Week 24.	
Reporting group title	JNJ-56136379- 75 mg + NA
Reporting group description:	
Subjects received 3*25 mg tablets of JNJ-56136379 plus 1 tablet of NA (0.5 mg ETV or 300 mg TDF) once daily from Day 1 to Week 24.	
Reporting group title	JNJ-56136379- 250 mg (Open label)
Reporting group description:	
Subjects received 2*100 mg and 2*25 mg tablets of JNJ-56136379 once daily during the open-label phase from Day 1 to Week 24.	
Reporting group title	Placebo (matching to JNJ-56136379 250 mg) + NA
Reporting group description:	
Subjects received 2 tablets of matching placebo plus 1 tablet of NA (0.5 mg ETV or 300 mg TDF) once daily from Day 1 to Week 24.	
Reporting group title	JNJ-56136379- 250 mg + NA
Reporting group description:	
Subjects received 2*100 mg and 2*25 mg tablets of JNJ-56136379 plus 1 tablet of NA (0.5 mg ETV or 300 mg TDF) once daily from Day 1 to Week 24.	
Subject analysis set title	Placebo + NA (Pooled)
Subject analysis set type	Safety analysis
Subject analysis set description:	
This analysis set includes subjects who received tablets of matching placebo to JNJ-56136379- 75 mg and JNJ-56136379- 250 mg respectively along with 1 tablet of NA (0.5 mg entecavir [ETV] or 300 mg tenofovir disoproxil fumarate [TDF])	
Subject analysis set title	JNJ-56136379 + NA (Pooled)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects in this analysis set included subjects from both JNJ56136379 75mg+ NA and JNJ56136379 250mg+ NA arms respectively	
Subject analysis set title	JNJ-56136379 75mg + ETV (Currently not treated)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Currently not treated subjects in this analysis set comprised of all those who were administered JNJ-56136379 75 mg along with the nucleot/side analog- ETV	
Subject analysis set title	JNJ-56136379 75mg + TDF (Currently not treated)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Currently not treated subjects in this analysis set comprised of all those who were administered JNJ-56136379 75 mg along with the nucleot/side analog- TDF	
Subject analysis set title	JNJ-56136379 75mg + ETV (virologically suppressed)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Virologically- suppressed subjects in this analysis set comprised of all those who were administered JNJ-56136379 75 mg along with the nucleot/side analog- ETV	
Subject analysis set title	JNJ-56136379 75mg + TDF (virologically suppressed)

Subject analysis set type	Sub-group analysis

Subject analysis set description:

Virologically- suppressed subjects in this analysis set comprised of all those who were administered JNJ-56136379 75 mg along with the nucleot/side analog- TDF

Subject analysis set title	JNJ-56136379 250 mg+ ETV (Currently not treated)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Currently not treated subjects in this analysis set comprised of all those who were administered JNJ-56136379 250 mg along with the nucleot/side analog- ETV

Subject analysis set title	JNJ-56136379 250 mg + TDF (Currently not treated)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Currently not treated subjects in this analysis set comprised of all those who were administered JNJ-56136379 250 mg along with the nucleot/side analog- TDF

Subject analysis set title	JNJ-56136379 250 mg + ETV (virologically suppressed)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Virologically- suppressed subjects in this analysis set comprised of all those who were administered JNJ-56136379 250 mg along with the nucleot/side analog- ETV

Subject analysis set title	JNJ-56136379 250 mg + TDF (virologically suppressed)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Virologically- suppressed subjects in this analysis set comprised of all those who were administered JNJ-56136379 250 mg along with the nucleot/side analog- TDF

Subject analysis set title	Placebo + ETV (virologically suppressed)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects in this analysis set received JNJ-56136379 75 mg placebo along with ETV.

Subject analysis set title	Placebo 75 mg + TDF (virologically suppressed)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Virologically suppressed subjects in this analysis set received placebo of JNJ-56136379 75 mg along with TDF

Subject analysis set title	Placebo 250 mg + TDF (virologically suppressed)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Virologically suppressed subjects in this analysis set received placebo of JNJ-56136379 250 mg along with TDF

Subject analysis set title	Placebo + NA (Pooled) [Virologically Suppressed Subjects]
Subject analysis set type	Intention-to-treat

Subject analysis set description:

This analysis set includes virologically suppressed subjects who received tablets of matching placebo to JNJ-56136379- 75 mg and JNJ-56136379- 250 mg respectively along with 1 tablet of NA (0.5 mg entecavir [ETV] or 300 mg tenofovir disoproxil fumarate [TDF])

Subject analysis set title	JNJ-56136379 75mg + NA (Virologically Suppressed Subjects)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Virologically- suppressed subjects in this analysis set comprised of all those who were administered JNJ-56136379 75 mg along with the nucleot/side analog

Subject analysis set title	JNJ-56136379 250 mg + NA (Virologically Suppressed Subjects)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Virologically- suppressed subjects in this analysis set comprised of all those who were administered JNJ-56136379 250 mg along with the nucleot/side analog

Subject analysis set title	JNJ-56136379 75 mg + NA (HbeAg Positive)

Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects in this analysis set comprised of all HbeAg positive subjects who received JNJ-56136379 75 mg+ NA treatment	
Subject analysis set title	JNJ-56136379 250 mg + NA (HbeAg positive)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects in this analysis set comprised of HbeAg positive subjects who received JNJ-56136379 250 mg+ NA treatment.	
Subject analysis set title	JNJ-56136379 75 mg + NA (HbeAg negative)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects in this analysis set comprised of HbeAg negative subjects who received JNJ-56136379 75 mg + NA treatment.	
Subject analysis set title	JNJ-56136379 250 mg + NA (HbeAg negative)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects in this analysis set comprised of HbeAg negative subjects who received JNJ-56136379 250 mg + NA treatment.	

Primary: Change From Baseline in Hepatitis B Surface Antigen (HBsAg) Levels at Week 24

End point title	Change From Baseline in Hepatitis B Surface Antigen (HBsAg) Levels at Week 24[1][2]
End point description:	
Change from baseline in HBsAg levels at Week 24 was assessed. Intent-to-Treat Population (ITT) consisted of all subjects who are randomized and received at least one dose of any study agent. If a subject received a study agent other than their randomly assigned study agent, subjects would be shown in the treatment arm as randomized. Here "n" represents number of subjects evaluable for the specified category.	
End point type	Primary
End point timeframe:	
Baseline and Week 24	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Endpoint was descriptive in nature, no inferential analysis 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: Endpoint was planned to be reported for specified arms only.

End point values	JNJ-56136379-75 mg (Open label)	JNJ-56136379-75 mg + NA	JNJ-56136379-250 mg (Open label)	JNJ-56136379-250 mg + NA
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	66	32	63
Units: log10 IU per milliliter (log10 IU/mL)				
arithmetic mean (standard deviation)				
HBeAg Positive (n=21,21,8,14,13)	-0.096 (± 0.3567)	-0.108 (± 0.2957)	-0.203 (± 0.4721)	-0.165 (± 0.4491)
HBeAg Negative: (n= 45,38,13,16,28)	0.053 (± 0.2066)	0.010 (± 0.0852)	0.064 (± 0.0913)	0.090 (± 0.1190)

End point values	Placebo + NA (Pooled)			
Subject group type	Subject analysis set			
Number of subjects analysed	43			
Units: log10 IU per milliliter (log10 IU/mL)				
arithmetic mean (standard deviation)				
HBeAg Positive (n=21,21,8,14,13)	-0.152 (± 0.2827)			
HBeAg Negative: (n= 45,38,13,16,28)	0.020 (± 0.0785)			

Statistical analyses

No statistical analyses for this end point

Primary: Posterior Probability of JNJ6379+NA over Placebo+NA for HBsAg Change from Baseline (log10) at Week 24 by Hepatitis B e Antigen Status for Currently not Treated Subjects

End point title	Posterior Probability of JNJ6379+NA over Placebo+NA for HBsAg Change from Baseline (log10) at Week 24 by Hepatitis B e Antigen Status for Currently not Treated Subjects[3]

End point description:

Posterior Probability of JNJ6379+NA over Placebo+NA for HBsAg change from baseline (log10) at Week 24 by Hepatitis B e antigen status for currently not Treated Subjects was analyzed using Bayesian approach.

End point type	Primary

End point timeframe:

Week 24

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: Endpoint was descriptive in nature, no inferential analysis was performed.

End point values	JNJ-56136379 75 mg + NA (HbeAg Positive)	JNJ-56136379 250 mg + NA (HbeAg positive)	JNJ-56136379 75 mg + NA (HbeAg negative)	JNJ-56136379 250 mg + NA (HbeAg negative)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	13	21	20
Units: Probability				
number (not applicable)	0	4.8	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Posterior Probability of JNJ6379+NA over Placebo+NA for HBsAg Change from Baseline (log10) at Week 24 by Hepatitis B e Antigen Status for Virologically Suppressed Subjects

End point title	Posterior Probability of JNJ6379+NA over Placebo+NA for

	HBsAg Change from Baseline (log10) at Week 24 by Hepatitis B e Antigen Status for Virologically Suppressed Subjects[4]

End point description:

Posterior probability of JNJ6379+NA over Placebo+NA for HBsAg change from baseline (log10) at Week 24 by Hepatitis B e antigen status for virologically suppressed subjects was analyzed using Bayesian approach.

End point type	Primary

End point timeframe:

Week 24

Notes:

[4] - 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: Endpoint was descriptive in nature, no inferential analysis was performed.

End point values	JNJ-56136379 75mg + NA (Virologically Suppressed Subjects)	JNJ-56136379 250 mg + NA (Virologically Suppressed Subjects)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	33	30		
Units: Probability				
number (not applicable)				
HbeAg Negative	0	0		
HbeAg Positive	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment- emergent Adverse Events (AEs)

End point title	Number of Subjects With Treatment- emergent Adverse Events (AEs)[5]

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. The safety population included all subjects who received at least one dose of the study agent; all safety endpoints were analyzed by the treatment arm as treated.

End point type	Secondary

End point timeframe:

Up to Week 80

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: Endpoint was planned to be reported for specified arms only.

End point values	JNJ-56136379-75 mg (Open label)	JNJ-56136379-75 mg + NA	JNJ-56136379-250 mg (Open label)	JNJ-56136379-250 mg + NA
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	66	32	63
Units: Subjects	18	55	25	54

End point values	Placebo + NA (Pooled)			
Subject group type	Subject analysis set			
Number of subjects analysed	43			
Units: Subjects	34			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Serious Adverse Events (SAEs)

End point title	Number of Subjects With Serious Adverse Events (SAEs)[6]

End point description:

A serious adverse event (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. The safety population included all subjects who received at least one dose of the study agent; all safety endpoints were analyzed by the treatment arm as treated.

End point type	Secondary

End point timeframe:

Up to Week 80

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: Endpoint was planned to be reported for specified arms only.

End point values	JNJ-56136379-75 mg (Open label)	JNJ-56136379-75 mg + NA	JNJ-56136379-250 mg (Open label)	JNJ-56136379-250 mg + NA
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	66	32	63
Units: Subjects	0	3	0	4

End point values	Placebo + NA (Pooled)			
Subject group type	Subject analysis set			
Number of subjects analysed	43			
Units: Subjects	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Clinically Significant Changes in Vital Signs, Physical Examinations, Electrocardiogram (ECG), and Laboratory Findings

End point title	Number of Subjects with Clinically Significant Changes in Vital Signs, Physical Examinations, Electrocardiogram (ECG), and Laboratory Findings[7]

End point description:

Number of subjects with clinically significant changes in vital signs, physical examinations, ECG, and laboratory findings were assessed. The safety population included all subjects who received at least one dose of the study agent; all safety endpoints were analyzed by the treatment arm as treated.

End point type	Secondary

End point timeframe:

Up to Week 80

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: Endpoint was planned to be reported for specified arms only.

End point values	JNJ-56136379-75 mg (Open label)	JNJ-56136379-75 mg + NA	JNJ-56136379-250 mg (Open label)	JNJ-56136379-250 mg + NA
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	66	32	63
Units: Subjects	0	0	0	0

End point values	Placebo + NA (Pooled)			
Subject group type	Subject analysis set			
Number of subjects analysed	43			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With HBsAg Levels Less Than (<) 1,000 or <100 International Units Per Milliliter (IU/mL) for Currently not Treated Subjects at Week 24

End point title	Percentage of Subjects With HBsAg Levels Less Than (<) 1,000 or <100 International Units Per Milliliter (IU/mL) for Currently not Treated Subjects at Week 24[8]

End point description:

Percentage of subjects with HBsAg levels less than (<) 1,000 or <100 IU/mL for currently not treated subjects at week 24 was assessed. Intent-to-treat (ITT) population: all participants who were randomized and received at least one dose of any study agent. If a participant received a study agent other than their randomly assigned study agent, participants were shown in the treatment arm as randomized.

End point type	Secondary

End point timeframe:

Week 24

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: Endpoint was planned to be reported for specified arms only.

End point values	JNJ-56136379-75 mg (Open label)	JNJ-56136379-75 mg + NA	JNJ-56136379-250 mg (Open label)	JNJ-56136379-250 mg + NA
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	33	32	33
Units: Percentage of subjects				
number (not applicable)				
HBsAg<100 IU/mL: HBeAg positive (n=8,12,14,11,8)	0	0	0	0
HBsAg<1000 IU/mL: HBeAg positive(n=13,21,16,19,13)	0	0	0	0
HBsAg<100 IU/mL: HBeAg negative (n=13,21,16,19,13)	0	0	0	0
HBsAg<1000 IU/mL:HBeAg negative (n=13,21,16,19,13)	23.1	4.8	0	10.5

End point values	Placebo + NA (Pooled)			
Subject group type	Subject analysis set			
Number of subjects analysed	22			
Units: Percentage of subjects				
number (not applicable)				
HBsAg<100 IU/mL: HBeAg positive (n=8,12,14,11,8)	0			
HBsAg<1000 IU/mL: HBeAg positive(n=13,21,16,19,13)	0			
HBsAg<100 IU/mL: HBeAg negative (n=13,21,16,19,13)	0			
HBsAg<1000 IU/mL:HBeAg negative (n=13,21,16,19,13)	15.4			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With HBsAg Levels Less Than (<) 1,000 or <100 International Units Per Milliliter (IU/mL) for Virologically Suppressed Subjects at Week 24

End point title	Percentage of Subjects With HBsAg Levels Less Than (<) 1,000 or <100 International Units Per Milliliter (IU/mL) for Virologically Suppressed Subjects at Week 24

End point description:

Percentage of subjects with HBsAg levels less than (<) 1,000 or <100 IU/mL for virologically suppressed subjects at week 24 was assessed. Intent-to-treat (ITT) population: all participants who were randomized and received at least one dose of any study agent. If a participant received a study agent other than their randomly assigned study agent, participants were shown in the treatment arm as randomized.

End point type	Secondary

End point timeframe:

Week 24

End point values	Placebo + NA (Pooled) [Virologically Suppressed Subjects]	JNJ-56136379 75mg + NA (Virologically Suppressed Subjects)	JNJ-56136379 250 mg + NA (Virologically Suppressed Subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	21	33	30	
Units: Percentage of subjects				
number (not applicable)				
HBsAg<100 IU/mL: HBeAg positive (n=5,9,10)	0	0	0	
HBsAg<1000 IU/mL: HBeAg positive (n=5,9,10)	20	11.1	10	
HBsAg<100 IU/mL: HBeAg negative (n=15,24,19)	0	0	0	
HBsAg<1000 IU/mL: HBeAg negative (n=15,24,19)	0	29.2	15.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Greater Than (>) 0.5 log10 IU/mL Reduction in HBsAg From Baseline for Currently-not Treated Subjects at Week 24

End point title	Percentage of Subjects With Greater Than (>) 0.5 log10 IU/mL Reduction in HBsAg From Baseline for Currently-not Treated Subjects at Week 24[9]

End point description:

Percentage of subjects with >0.5 log10 IU/mL reduction in HBsAg from baseline for currently not treated subjects at week 24 was assessed. Intent-to-treat (ITT) population: all participants who were randomized and received at least one dose of any study agent. If a participant received a study agent other than their randomly assigned study agent, participants were shown in the treatment arm as randomized.

End point type	Secondary

End point timeframe:

Week 24

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: Endpoint was planned to be reported for specified arms only.

End point values	JNJ-56136379-75 mg (Open label)	JNJ-56136379-75 mg + NA	JNJ-56136379-250 mg (Open label)	JNJ-56136379-250 mg + NA
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	12	14	11
Units: Percentage of subjects				
number (not applicable)	12.5	8.3	28.6	36.4

End point values	Placebo + NA (Pooled)			
Subject group type	Subject analysis set			
Number of subjects analysed	8			
Units: Percentage of subjects				
number (not applicable)	12.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Greater Than (>) 0.5 log10 IU/mL Reduction in HBsAg From Baseline for Virologically Suppressed Subjects at Week 24

End point title	Percentage of Subjects With Greater Than (>) 0.5 log10 IU/mL Reduction in HBsAg From Baseline for Virologically Suppressed Subjects at Week 24

End point description:

Percentage of subjects with >0.5 log10 IU/mL reduction in HBsAg from baseline for virologically suppressed subjects at week 24 was assessed. Intent-to-treat (ITT) population: all participants who were randomized and received at least one dose of any study agent. If a participant received a study agent other than their randomly assigned study agent, participants were shown in the treatment arm as randomized.

End point type	Secondary

End point timeframe:

Week 24

End point values	Placebo + NA (Pooled) [Virologically Suppressed Subjects]	JNJ-56136379 75mg + NA (Virologically Suppressed Subjects)	JNJ-56136379 250 mg + NA (Virologically Suppressed Subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	9	10	
Units: Percentage of subjects				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hepatitis B Virus (HBV) Deoxyribonucleic acid (DNA) Levels at Week 24 for Currently not Treated HbeAg Positive Subjects

End point title	Change From Baseline in Hepatitis B Virus (HBV) Deoxyribonucleic acid (DNA) Levels at Week 24 for Currently

	not Treated HbeAg Positive Subjects[10]

End point description:

Change from baseline in HBV DNA levels at week 24 for currently not treated HBeAg positive subjects was assessed. Intent-to-treat (ITT) population: all participants who were randomized and received at least one dose of any study agent. If a participant received a study agent other than their randomly assigned study agent, participants were shown in the treatment arm as randomized.

End point type	Secondary

End point timeframe:

Baseline and Week 24

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: Endpoint was planned to be reported for specified arms only.

End point values	JNJ-56136379-75 mg (Open label)	JNJ-56136379-75 mg + NA	JNJ-56136379-250 mg (Open label)	JNJ-56136379-250 mg + NA
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	12	14	11
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-3.284 (± 2.1148)	-5.531 (± 0.7915)	-5.719 (± 0.8395)	-5.883 (± 1.1396)

End point values	Placebo + NA (Pooled)			
Subject group type	Subject analysis set			
Number of subjects analysed	8			
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-5.211 (± 1.1986)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hepatitis B Virus (HBV) Deoxyribonucleic acid (DNA) Levels at Week 24 for Currently not Treated HbeAg Negative Subjects

End point title	Change From Baseline in Hepatitis B Virus (HBV) Deoxyribonucleic acid (DNA) Levels at Week 24 for Currently not Treated HbeAg Negative Subjects[11]

End point description:

Change from baseline in HBV DNA levels at week 24 for currently not treated HBeAg negative subjects was assessed. Intent-to-treat (ITT) population: all participants who were randomized and received at least one dose of any study agent. If a participant received a study agent other than their randomly assigned study agent, participants were shown in the treatment arm as randomized.

End point type	Secondary

End point timeframe:

Baseline up to Week 24

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: Endpoint was planned to be reported for specified arms only.

End point values	JNJ-56136379-75 mg (Open label)	JNJ-56136379-75 mg + NA	JNJ-56136379-250 mg (Open label)	JNJ-56136379-250 mg + NA
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	21	18	20
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-3.469 (± 1.2901)	-4.077 (± 0.9435)	-3.545 (± 1.1482)	-3.690 (± 1.5289)

End point values	Placebo + NA (Pooled)			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-3.622 (± 1.3003)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Undetectable HBV DNA Levels at Week 24 for Currently not Treated Population

End point title	Percentage of Subjects With Undetectable HBV DNA Levels at Week 24 for Currently not Treated Population[12]

End point description:

Percentage of subjects with undetectable HBV DNA levels at week 24 for currently not treated population was evaluated. Intent-to-treat (ITT) population: all participants who were randomized and received at least one dose of any study agent. If a participant received a study agent other than their randomly assigned study agent, participants were shown in the treatment arm as randomized. Here "n" represents number of subjects evaluable for the specified category.

End point type	Secondary

End point timeframe:

Week 24

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: Endpoint was planned to be reported for specified arms only.

End point values	JNJ-56136379-75 mg (Open label)	JNJ-56136379-75 mg + NA	JNJ-56136379-250 mg (Open label)	JNJ-56136379-250 mg + NA
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	66	32	63
Units: Percentage of subjects				
number (not applicable)				
HBeAg Positive (n= 12,12,14,23,8)	0	0	0	7.7
HBeAg Negative (n= 16,21,18,20,14)	12.5	33.3	38.9	35.0

End point values	Placebo + NA (Pooled)			
Subject group type	Subject analysis set			
Number of subjects analysed	22			
Units: Percentage of subjects				
number (not applicable)				
HBeAg Positive (n= 12,12,14,23,8)	0			
HBeAg Negative (n= 16,21,18,20,14)	35.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Undetectable HBV DNA Levels at Week 24 for Virologically Suppressed Population

End point title	Percentage of Subjects With Undetectable HBV DNA Levels at Week 24 for Virologically Suppressed Population

End point description:

Percentage of subjects with undetectable HBV DNA levels at week 24 for virologically suppresed subjects was evaluated. Intent-to-treat (ITT) population: all participants who were randomized and received at least one dose of any study agent. If a participant received a study agent other than their randomly assigned study agent, participants were shown in the treatment arm as randomized. Here "n" represents number of subjects evaluable for the specified category.

End point type	Secondary

End point timeframe:

Week 24

End point values	Placebo + NA (Pooled) [Virologically Suppressed Subjects]	JNJ-56136379 75mg + NA (Virologically Suppressed Subjects)	JNJ-56136379 250 mg + NA (Virologically Suppressed Subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	21	33	30	
Units: Percentage of subjects				
number (not applicable)				
HBeAg positive (n= 6,9,10)	50	66.7	90	

HBeAg negative (n= 15,24,20)	100	100	90	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hepatitis B E Antigen (HBeAg) Levels for HBeAg Positive Subjects at Week 24

End point title	Change From Baseline in Hepatitis B E Antigen (HBeAg) Levels for HBeAg Positive Subjects at Week 24[13]

End point description:

Change from baseline in HBeAg levels for HBeAg positive subjects at week 24 was assessed. Intent-to-treat (ITT) population: all participants who were randomized and received at least one dose of any study agent. If a participant received a study agent other than their randomly assigned study agent, participants were shown in the treatment arm as randomized.

End point type	Secondary

End point timeframe:

Baseline up to Week 24

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: Endpoint was planned to be reported for specified arms only.

End point values	JNJ-56136379-75 mg (Open label)	JNJ-56136379-75 mg + NA	JNJ-56136379-250 mg (Open label)	JNJ-56136379-250 mg + NA
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	21	14	21
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-0.456 (± 0.2908)	-0.413 (± 0.3793)	-0.974 (± 0.8400)	-0.445 (± 0.5618)

End point values	Placebo + NA (Pooled)			
Subject group type	Subject analysis set			
Number of subjects analysed	13			
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-0.619 (± 0.7248)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects by HBeAg Levels Reduced from Baseline >0.5 log10 IU/mL and >1 log10 IU/mL for Currently not Treated Subjects at Week 24

End point title	Percentage of Subjects by HBeAg Levels Reduced from Baseline >0.5 log10 IU/mL and >1 log10 IU/mL for Currently not Treated Subjects at Week 24[14]

End point description:

Percentage of subjects by HBeAg levels reduced from baseline >0.5 log10 IU/mL and >1 log10 IU/mL for currently not treated subjects at week 24 was evaluated. Intent-to-treat (ITT) population: all participants who were randomized and received at least one dose of any study agent. If a participant received a study agent other than their randomly assigned study agent, participants were shown in the treatment arm as randomized.

End point type	Secondary

End point timeframe:

Week 24

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: Endpoint was planned to be reported for specified arms only.

End point values	JNJ-56136379-75 mg (Open label)	JNJ-56136379-75 mg + NA	JNJ-56136379-250 mg (Open label)	JNJ-56136379-250 mg + NA
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	12	14	11
Units: Percentage of subjects				
number (not applicable)				
Reduction from Baseline at Wk 24: >0.5 log10 IU/mL	50	41.7	78.6	63.6
Reduction from Baseline at Wk 24: >1 log10 IU/mL	0	8.3	42.9	36.4

End point values	Placebo + NA (Pooled)			
Subject group type	Subject analysis set			
Number of subjects analysed	8			
Units: Percentage of subjects				
number (not applicable)				
Reduction from Baseline at Wk 24: >0.5 log10 IU/mL	62.5			
Reduction from Baseline at Wk 24: >1 log10 IU/mL	37.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects by HBeAg Levels Reduced from Baseline >0.5 log10 IU/mL and >1 log10 IU/mL for Virologically Suppressed Subjects at Week 24

End point title	Percentage of Subjects by HBeAg Levels Reduced from Baseline >0.5 log10 IU/mL and >1 log10 IU/mL for Virologically Suppressed Subjects at Week 24

End point description:

Percentage of subjects by HBeAg levels reduced from baseline >0.5 log10 IU/mL and >1 log10 IU/mL for virologically suppressed subjects at week 24 was evaluated. Intent-to-treat (ITT) population: all participants who were randomized and received at least one dose of any study agent. If a participant received a study agent other than their randomly assigned study agent, participants were shown in the treatment arm as randomized.

End point type	Secondary

End point timeframe:

Week 24

End point values	Placebo + NA (Pooled) [Virologically Suppressed Subjects]	JNJ-56136379 75mg + NA (Virologically Suppressed Subjects)	JNJ-56136379 250 mg + NA (Virologically Suppressed Subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	9	10	
Units: Percentage of subjects				
number (not applicable)				
Reduction from Baseline at Wk 24: >0.5 log10 IU/mL	20	33.3	10	
Reduction from Baseline at Wk 24: >1 log10 IU/mL	20	11.1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With HBsAg Seroclearance

End point title	Number of Subjects With HBsAg Seroclearance[15]

End point description:

Number of subjects with HBsAg seroclearance was assessed. Intent-to-treat (ITT) population: all participants who were randomized and received at least one dose of any study agent. If a participant received a study agent other than their randomly assigned study agent, participants were shown in the treatment arm as randomized.

End point type	Secondary

End point timeframe:

Week 24

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: Endpoint was planned to be reported for specified arms only.

End point values	JNJ-56136379-75 mg (Open label)	JNJ-56136379-75 mg + NA	JNJ-56136379-250 mg (Open label)	JNJ-56136379-250 mg + NA
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	66	32	63
Units: Subjects				
Week 24	0	0	0	0

End point values	Placebo + NA (Pooled)	Placebo + NA (Pooled) [Virologically Suppressed Subjects]	JNJ-56136379 75mg + NA (Virologically Suppressed Subjects)	JNJ-56136379 250 mg + NA (Virologically Suppressed Subjects)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	43	21	33	30
Units: Subjects				
Week 24	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With HBsAg Seroconversion

End point title	Number of Subjects With HBsAg Seroconversion[16]

End point description:

Number of subjects with HBsAg seroconversion was assessed. Intent-to-treat (ITT) population: all participants who were randomized and received at least one dose of any study agent. If a participant received a study agent other than their randomly assigned study agent, participants were shown in the treatment arm as randomized.

End point type	Secondary

End point timeframe:

Week 24

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: Endpoint was planned to be reported for specified arms only.

End point values	JNJ-56136379-75 mg (Open label)	JNJ-56136379-75 mg + NA	JNJ-56136379-250 mg (Open label)	JNJ-56136379-250 mg + NA
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	66	32	63
Units: Subjects				
Week 24	0	0	0	0

End point values	Placebo + NA (Pooled)	Placebo + NA (Pooled) [Virologically Suppressed Subjects]		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	43	21		
Units: Subjects				
Week 24	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Normalized Alanine Aminotransferase (ALT) Levels for Currently not Treated Population at Week 24

End point title	Percentage of Subjects With Normalized Alanine Aminotransferase (ALT) Levels for Currently not Treated Population at Week 24[17]

End point description:

Percentage of subjects with normalized alanine aminotransferase (ALT) levels for currently not treated population at week 24 was assessed ,whose ALT levels were above upper limit of normal at baseline. Safety population: all participants who received at least one dose of the study agent; all safety endpoints were analyzed by the treatment arm as treated. Here "n" represents number of subjects evaluable for the specified category.

End point type	Secondary

End point timeframe:

Week 24

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: Endpoint was planned to be reported for specified arms only.

End point values	JNJ-56136379-75 mg (Open label)	JNJ-56136379-75 mg + NA	JNJ-56136379-250 mg (Open label)	JNJ-56136379-250 mg + NA
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	27	26	27
Units: Percentage of subjects				
number (not applicable)				
HBeAg positive (n=8,11,14,11,8)	60	54.5	64.3	44.4
HBeAg negative (n=15,16,12,16,10)	91.7	68.8	72.7	80

End point values	Placebo + NA (Pooled)			
Subject group type	Subject analysis set			
Number of subjects analysed	18			
Units: Percentage of subjects				
number (not applicable)				
HBeAg positive (n=8,11,14,11,8)	62.5			
HBeAg negative (n=15,16,12,16,10)	55.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Normalized Alanine Aminotransferase (ALT) Levels for Virologically Suppressed Population at Week 24

End point title	Percentage of Subjects With Normalized Alanine Aminotransferase (ALT) Levels for Virologically Suppressed Population at Week 24

End point description:

Percentage of subjects with normalized alanine aminotransferase (ALT) levels for virologically suppressed population at week 24 was assessed ,whose ALT levels were above upper limit of normal at baseline. Safety population: all participants who received at least one dose of the study agent; all safety endpoints were analyzed by the treatment arm as treated. Here "n" represents number of subjects evaluable for the specified category.

End point type	Secondary

End point timeframe:

Week 24

End point values	Placebo + NA (Pooled) [Virologically Suppressed Subjects]	JNJ-56136379 75mg + NA (Virologically Suppressed Subjects)	JNJ-56136379 250 mg + NA (Virologically Suppressed Subjects)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	3	4	5	
Units: Percentage of subjects				
number (not applicable)				
HBeAg Positive (n= 1,1,3)	0	100	33.3	
HBeAg Negative (n= 2,3,2)	50	100	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Virological Breakthrough

End point title	Number of Subjects With Virological Breakthrough[18]

End point description:

Number of subjects with viral breakthrough defined as confirmed on treatment HBV DNA increase by greater than (>) 1 log10 from nadir level or confirmed on treatment level >200 International Units Per Milliliter (IU/mL) in participants who had HBV DNA level below the lower limit of quantification (LLOQ) of the HBV DNA assay. Intent-to-Treat Population (ITT) consisted of all subjects who are randomized and received at least one dose of any study agent. If a subject receives a study agent other than their randomly assigned study agent, subjects will be shown in the treatment arm as randomized.

End point type	Secondary

End point timeframe:

Up to Week 80

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: Endpoint was planned to be reported for specified arms only.

End point values	JNJ-56136379-75 mg (Open label)	JNJ-56136379-75 mg + NA	JNJ-56136379-250 mg (Open label)	JNJ-56136379-250 mg + NA
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	66	32	63
Units: Subjects				
Viral breakthrough during 24 weeks	5	0	1	0
Breakthrough b/w 25 & 48 weeks(n=3,43,20,48,33)	1	1	0	0
Breakthrough for NA treatment (n= 24,64,29,60,40)	0	2	2	2

End point values	Placebo + NA (Pooled)			
Subject group type	Subject analysis set			
Number of subjects analysed	43			
Units: Subjects				
Viral breakthrough during 24 weeks	0			
Breakthrough b/w 25 & 48 weeks(n=3,43,20,48,33)	0			
Breakthrough for NA treatment (n= 24,64,29,60,40)	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of Entecavir [ETV]

End point title	Plasma Concentrations of Entecavir [ETV]

End point description:

Plasma concentrations of ETV administered as monotherapy or co-administered with JNJ-56136379 was determined. The pharmacokinetic (PK) analysis set included data for all subjects with available plasma concentrations. "99999" denotes timepoints in particular arms which do not have any value.

End point type	Secondary

End point timeframe:

Day1: 0 hours (h), Day 1: 2h, Week (W)1: 0h, W2:0h, W4: 0h, W8: 0h, W12: 0h, W20: 0h, W24: 0h, W28: 0h, W32: 0h, W36: 0h, W44: 0h, W48: 0h, Follow-up (FU): W2, FU: W4

End point values	JNJ-56136379 75mg + ETV (Currently not treated)	JNJ-56136379 75mg + ETV (virologically suppressed)	JNJ-56136379 250 mg+ ETV (Currently not treated)	JNJ-56136379 250 mg + ETV (virologically suppressed)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	15	7	9
Units: nanograms per milliliter (ng/ml)				
arithmetic mean (standard deviation)				
D1: 0h	99999 (± 99999)	0.683 (± 0.414)	99999 (± 99999)	99999 (± 99999)

D1: 2h	1.39 (± 0.709)	1.86 (± 0.639)	1.18 (± 0.197)	1.89 (± 0.429)
W1: 0h	0.321 (± 0.0961)	0.464 (± 0.143)	0.289 (± 0.0351)	0.472 (± 0.120)
W2: 0h	0.285 (± 0.166)	0.469 (± 0.153)	0.377 (± 0.0531)	0.469 (± 0.0835)
W4: 0h	0.417 (± 0.143)	0.529 (± 0.198)	0.414 (± 0.0742)	0.539 (± 0.108)
W8: 0h	0.353 (± 0.226)	0.496 (± 0.179)	0.466 (± 0.0913)	0.493 (± 0.0816)
W12: 0h	0.467 (± 0.188)	0.454 (± 0.135)	0.479 (± 0.0650)	0.548 (± 0.0535)
W20: 0h	0.441 (± 0.147)	0.617 (± 0.408)	0.481 (± 0.0625)	0.537 (± 0.109)
W24: 0h	0.395 (± 0.309)	0.491 (± 0.144)	0.385 (± 0.0415)	0.576 (± 0.121)
W28: 0h	99999 (± 99999)	0.446 (± 0.148)	0.527 (± 0.0302)	0.519 (± 0.153)
W32: 0h	99999 (± 99999)	0.467 (± 0.201)	0.462 (± 0.0410)	0.489 (± 0.114)
W36: 0h	99999 (± 99999)	0.487 (± 0.185)	0.442 (± 0.0517)	0.526 (± 0.109)
W44: 0h	99999 (± 99999)	0.525 (± 0.177)	0.438 (± 0.0352)	0.517 (± 0.121)
W48: 0h	0.434 (± 0.0968)	0.554 (± 0.287)	0.539 (± 0.0414)	0.537 (± 0.105)
FU: W2	0.542 (± 0.311)	0.635 (± 0.449)	0.307 (± 0.176)	0.433 (± 0.117)
FU: W4	0.354 (± 0.260)	0.445 (± 0.164)	0.309 (± 0.161)	0.725 (± 0.598)

End point values	Placebo + ETV (virologically suppressed)			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: nanograms per milliliter (ng/ml)				
arithmetic mean (standard deviation)				
D1: 0h	99999 (± 99999)			
D1: 2h	99999 (± 99999)			
W1: 0h	1.94 (± 2.43)			
W2: 0h	0.871 (± 0.909)			
W4: 0h	0.647 (± 0.628)			
W8: 0h	99999 (± 99999)			
W12: 0h	0.277 (± 0.0733)			
W20: 0h	99999 (± 99999)			
W24: 0h	99999 (± 99999)			
W28: 0h	99999 (± 99999)			
W32: 0h	99999 (± 99999)			

W36: 0h	0.962 (± 1.07)			
W44: 0h	99999 (± 99999)			
W48: 0h	0.766 (± 0.594)			
FU: W2	99999 (± 99999)			
FU: W4	1.00 (± 1.13)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of Tenofovir (TFV) for Currently not Treated and Virologically Suppressed Population

End point title	Plasma Concentrations of Tenofovir (TFV) for Currently not Treated and Virologically Suppressed Population[19]

End point description:

Plasma concentrations of TFV for currently not treated and virologically suppressed population administered as monotherapy or co-administered with JNJ-56136379 was determined. The PK analysis set included data for all subjects with available plasma concentrations. "99999" denotes timepoints in particular arms which do not have any value.

End point type	Secondary

End point timeframe:

Day1: 0 hours (h), Day 1: 2h, Week (W)1: 0h, W2:0h, W4: 0h, W8: 0h, W12: 0h, W16: 0h, W20: 0h, W24: 0h, W28: 0h, W32: 0h, W36: 0h, W40: 0h, W44: 0h, W48: 0h, Follow-up (FU): W2, FU: W4

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: Endpoint was planned to be reported for specified arms only.

End point values	Placebo (matching JNJ-6379 75mg) + Nucleos(t)ide analog (NA)	Placebo (matching to JNJ-56136379 250 mg) + NA	JNJ-56136379 75mg + TDF (Currently not treated)	JNJ-56136379 75mg + TDF (virologically suppressed)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	9	8	24	18
Units: nanograms per milliliter (ng/ml)				
arithmetic mean (standard deviation)				
D1: 0h	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	68.9 (± 10.1)
D1: 2h	277 (± 116)	170 (± 114)	372 (± 478)	306 (± 145)
W1: 0h	79.6 (± 38.1)	92.7 (± 134)	92.6 (± 37.4)	97.9 (± 38.0)
W2: 0h	64.2 (± 34.5)	50.1 (± 14.1)	81.5 (± 22.6)	97.5 (± 34.0)
W4: 0h	62.9 (± 17.7)	46.5 (± 10.5)	90.2 (± 25.8)	96.9 (± 25.0)
W8: 0h	66.3 (± 23.7)	54.2 (± 18.3)	92.6 (± 25.7)	118 (± 48.0)
W12: 0h	67.5 (± 31.2)	51.3 (± 15.9)	93.5 (± 29.1)	99.4 (± 33.8)
W16: 0h	99999 (± 99999)	47.5 (± 25.4)	99999 (± 99999)	99999 (± 99999)
W20: 0h	72.6 (± 34.2)	51.2 (± 13.8)	85.8 (± 30.6)	120 (± 30.1)
W24: 0h	75.9 (± 51.0)	50.5 (± 20.1)	89.1 (± 30.1)	104 (± 29.9)
W28: 0h	74.4 (± 38.1)	51.2 (± 19.9)	99.0 (± 32.6)	110 (± 43.2)

W32: 0h	78.8 (± 59.6)	52.7 (± 26.1)	89.6 (± 37.1)	106 (± 36.4)
W36: 0h	78.9 (± 55.8)	42.5 (± 19.3)	96.0 (± 38.3)	101 (± 33.1)
W40: 0h	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
W44: 0h	86.3 (± 30.8)	46.3 (± 26.0)	81.8 (± 38.9)	109 (± 53.4)
W48: 0h	76.4 (± 40)	47.8 (± 18.6)	89.5 (± 49.8)	114 (± 31.7)
FU: W2	73.8 (± 37.1)	52.1 (± 17.3)	65.7 (± 29.5)	73.2 (± 18.5)
FU: W4	72.4 (± 32.1)	57.1 (± 13.6)	68.7 (± 54.3)	71.2 (± 33.0)

End point values	JNJ-56136379 250 mg + TDF (Currently not treated)	JNJ-56136379 250 mg + TDF (virologically suppressed)	Placebo 75 mg + TDF (virologically suppressed)	Placebo 250 mg + TDF (virologically suppressed)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	26	21	5	8
Units: nanograms per milliliter (ng/ml)				
arithmetic mean (standard deviation)				
D1: 0h	99999 (± 99999)	63.3 (± 27.4)	99999 (± 99999)	99999 (± 99999)
D1: 2h	249 (± 96.9)	364 (± 260)	274 (± 153)	311 (± 92.5)
W1: 0h	97.8 (± 27.7)	97.1 (± 36.8)	76.8 (± 40.8)	59.2 (± 15.7)
W2: 0h	97.6 (± 23.7)	114 (± 51.0)	82.0 (± 53.0)	65.9 (± 18.9)
W4: 0h	99.6 (± 26.4)	110 (± 41.4)	83.1 (± 54.8)	66.9 (± 20.3)
W8: 0h	108 (± 36.0)	109 (± 32.2)	84.0 (± 54.1)	65.5 (± 28.9)
W12: 0h	102 (± 35.3)	130 (± 87.8)	98.8 (± 73.6)	63.5 (± 21.6)
W16: 0h	77.8 (± 15.0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
W20: 0h	115 (± 41.7)	127 (± 64.9)	99.6 (± 85.0)	64.8 (± 23.3)
W24: 0h	99.3 (± 37.8)	113 (± 47.6)	78.3 (± 33.4)	73.8 (± 33.0)
W28: 0h	108 (± 39.0)	155 (± 107)	81.7 (± 37.7)	70.6 (± 28.1)
W32: 0h	88.5 (± 25.6)	139 (± 93.3)	75.5 (± 54.8)	61.2 (± 21.2)
W36: 0h	101 (± 34.2)	132 (± 90.2)	80.2 (± 50.3)	80.2 (± 31.2)
W40: 0h	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
W44: 0h	105 (± 33.5)	129 (± 73.6)	72.7 (± 54.9)	93.0 (± 64.2)
W48: 0h	100 (± 29.9)	133 (± 117)	87.6 (± 58.5)	66.2 (± 22.1)
FU: W2	73.5 (± 23.2)	136 (± 95.5)	86.5 (± 73.8)	51.9 (± 23.4)
FU: W4	68.4 (± 43.6)	95.8 (± 83.6)	74.7 (± 47.6)	59.7 (± 23.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of JNJ-56136379 for Currently not Treated and Virologically Suppressed Population

End point title	Plasma Concentrations of JNJ-56136379 for Currently not Treated and Virologically Suppressed Population[20]

End point description:

Plasma concentrations of JNJ-56136379 for currently not treated and virologically suppressed population administered as monotherapy or when co-administered with NA (ETV or TDF) was determined. The PK

analysis set included data for all subjects with available plasma concentrations. "99999" denotes timepoints in particular arms which do not have any value.

End point type	Secondary

End point timeframe:

Day1: 0 hours (h), Day 1: 2h, Week (W)1: 0h, W2:0h, W4: 0h, W8: 0h, W12: 0h, W16: 0h, W20: 0h, W24: 0h, W28: 0h, W32: 0h, W36: 0h, W40: 0h, W44: 0h, W48: 0h, Follow-up (FU): W2, FU: W4

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: Endpoint was planned to be reported for specified arms only.

End point values	JNJ-56136379-75 mg (Open label)	JNJ-56136379-250 mg (Open label)	JNJ-56136379 75mg + ETV (Currently not treated)	JNJ-56136379 75mg + TDF (Currently not treated)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	28	32	9	24
Units: nanograms per milliliter (ng/ml)				
arithmetic mean (standard deviation)				
D1: 0h	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
D1:2h	709 (± 307)	2143 (± 1300)	520 (± 279)	820 (± 306)
W1: 0h	2269 (± 597)	7339 (± 2040)	2264 (± 455)	2368 (± 695)
W2: 0h	3424 (± 845)	10894 (± 2631)	3094 (± 892)	3702 (± 1028)
W4: 0h	4116 (± 941)	12827 (± 3104)	4368 (± 1216)	4697 (± 1474)
W08: 0h	4617 (± 1195)	13697 (± 3702)	5006 (± 1258)	4719 (± 1465)
W12: 0h	4130 (± 1145)	12676 (± 3431)	4976 (± 1302)	4582 (± 1324)
W16: 0h	99999 (± 99999)	11333 (± 2639)	99999 (± 99999)	99999 (± 99999)
W20: 0h	3754 (± 1132)	12757 (± 4298)	4648 (± 1508)	4698 (± 1661)
W24: 0h	3613 (± 813)	12626 (± 3396)	4650 (± 1461)	4767 (± 1601)
W28:0h	4733 (± 350)	12025 (± 3229)	4300 (± 1355)	4439 (± 1446)
W32: 0h	99999 (± 99999)	12162 (± 2780)	4677 (± 646)	4825 (± 2429)
W36: 0h	99999 (± 99999)	11289 (± 2973)	4463 (± 1444)	4144 (± 1599)
W40: 0h	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
W44: 0h	99999 (± 99999)	11198 (± 2749)	4507 (± 1121)	3430 (± 1346)
W48: 0h	99999 (± 99999)	11797 (± 2482)	99999 (± 99999)	99999 (± 99999)
FU: W2	916 (± 930)	2459 (± 1529)	1330 (± 887)	909 (± 740)
FU: W4	242 (± 359)	494 (± 427)	320 (± 276)	226 (± 236)

End point values	JNJ-56136379 75mg + ETV (virologically suppressed)	JNJ-56136379 75mg + TDF (virologically suppressed)	JNJ-56136379 250 mg+ ETV (Currently not treated)	JNJ-56136379 250 mg + TDF (Currently not treated)

Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	18	7	26
Units: nanograms per milliliter (ng/ml)				
arithmetic mean (standard deviation)				
D1: 0h	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
D1:2h	857 (± 238)	616 (± 385)	2287 (± 946)	2021 (± 893)
W1: 0h	2144 (± 553)	2301 (± 639)	6461 (± 2014)	7138 (± 2280)
W2: 0h	3193 (± 1017)	3206 (± 710)	9381 (± 2168)	10588 (± 3568)
W4: 0h	3689 (± 1178)	3694 (± 815)	10760 (± 2162)	12513 (± 4229)
W08: 0h	3917 (± 1131)	3998 (± 1376)	11027 (± 2009)	13037 (± 4394)
W12: 0h	4194 (± 1279)	3813 (± 945)	11347 (± 1754)	12524 (± 4756)
W16: 0h	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	12316 (± 1947)
W20: 0h	3948 (± 1151)	4134 (± 1375)	10517 (± 2031)	11425 (± 3719)
W24: 0h	3989 (± 957)	3836 (± 1160)	10888 (± 1576)	11625 (± 5087)
W28:0h	4259 (± 1083)	3506 (± 1032)	11753 (± 2719)	11746 (± 4752)
W32: 0h	3788 (± 841)	3721 (± 1088)	9840 (± 3770)	12119 (± 4062)
W36: 0h	3801 (± 1170)	3535 (± 964)	11350 (± 3439)	11192 (± 5191)
W40: 0h	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
W44: 0h	3998 (± 1139)	3784 (± 1056)	11570 (± 2674)	11016 (± 4277)
W48: 0h	3918 (± 1259)	99999 (± 99999)	11220 (± 2464)	10740 (± 2400)
FU: W2	621 (± 607)	912 (± 585)	1922 (± 1628)	2192 (± 1535)
FU: W4	89.8 (± 102)	204 (± 209)	572 (± 624)	1025 (± 1523)

End point values	JNJ-56136379 250 mg + ETV (virologically suppressed)	JNJ-56136379 250 mg + TDF (virologically suppressed)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	9	21		
Units: nanograms per milliliter (ng/ml)				
arithmetic mean (standard deviation)				
D1: 0h	99999 (± 99999)	99999 (± 99999)		
D1:2h	2103 (± 1400)	2083 (± 1022)		
W1: 0h	5758 (± 1081)	7280 (± 2098)		
W2: 0h	8485 (± 2269)	10077 (± 2886)		
W4: 0h	10106 (± 2838)	12167 (± 4271)		
W08: 0h	11295 (± 3829)	13352 (± 6072)		

W12: 0h	10404 (± 4246)	12776 (± 5191)		
W16: 0h	99999 (± 99999)	99999 (± 99999)		
W20: 0h	10761 (± 3980)	12432 (± 4249)		
W24: 0h	10219 (± 3370)	11542 (± 4612)		
W28:0h	9959 (± 2929)	11344 (± 4482)		
W32: 0h	10189 (± 3160)	12099 (± 6301)		
W36: 0h	10036 (± 2786)	12227 (± 5396)		
W40: 0h	99999 (± 99999)	99999 (± 99999)		
W44: 0h	9634 (± 3707)	14853 (± 7977)		
W48: 0h	99999 (± 99999)	15080 (± 8060)		
FU: W2	1919 (± 1359)	3190 (± 4462)		
FU: W4	389 (± 384)	1066 (± 2319)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-Associated Mutations

End point title	Number of Subjects With Treatment-Associated Mutations[21]

End point description:

Viral genome sequence analysis was performed to evaluate emergence of mutations associated with JNJ-56136379 considering 15 HBV core protein positions of interest. Intent-to-treat (ITT) population: all participants who were randomized and received at least one dose of any study agent. If a participant received a study agent other than their randomly assigned study agent, participants were shown in the treatment arm as randomized. Here number of subjects analyzed corresponds to the number of subjects with paired baseline and post-baseline sequence info available.

End point type	Secondary

End point timeframe:

Up to Week 80

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: Endpoint was planned to be reported for specified arms only.

End point values	JNJ-56136379-75 mg (Open label)	JNJ-56136379-75 mg + NA	JNJ-56136379-250 mg (Open label)	JNJ-56136379-250 mg + NA
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	22	17	14
Units: Subjects				
Emergence of mutations during 24 weeks	8	0	4	0
Emergence of mutations between 25 and 48 weeks	2	0	0	0

Emergence of mutations on NA treatment	0	0	0	0

End point values	Placebo + NA (Pooled)			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: Subjects				
Emergence of mutations during 24 weeks	0			
Emergence of mutations between 25 and 48 weeks	0			
Emergence of mutations on NA treatment	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 104 weeks	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups	
Reporting group title	JNJ-56136379-75 mg (Open label)
Reporting group description:	
Subjects currently not treated received 3*25 milligrams (mg) tablets of JNJ-56136379 once daily during the open label phase from Day 1 to Week 24.	
Reporting group title	Placebo (matching JNJ-6379 75 mg) + Nucleos(t)ide analog (NA)
Reporting group description:	
Subjects received 3 tablets of matching placebo plus 1 tablet of NA (0.5 mg entecavir [ETV] or 300 mg tenofovir disoproxil fumarate [TDF]) once daily from Day 1 to Week 24.	
Reporting group title	JNJ-56136379- 75 mg + NA
Reporting group description:	
Subjects received 3*25 mg tablets of JNJ-56136379 plus 1 tablet of NA (0.5 mg ETV or 300 mg TDF) once daily from Day 1 to Week 24.	
Reporting group title	JNJ-56136379- 250 mg (Open label)
Reporting group description:	
Subjects received 2*100 mg and 2*25 mg tablets of JNJ-56136379 once daily during the open-label phase from Day 1 to Week 24.	
Reporting group title	Placebo (matching to JNJ-56136379 250 mg) + NA
Reporting group description:	
Subjects received 2 tablets of matching placebo plus 1 tablet of NA (0.5 mg ETV or 300 mg TDF) once daily from Day 1 to Week 24.	
Reporting group title	JNJ-56136379- 250 mg + NA
Reporting group description:	
Subjects received 2*100 mg and 2*25 mg tablets of JNJ-56136379 plus 1 tablet of NA (0.5 mg ETV or 300 mg TDF) once daily from Day 1 to Week 24.	

Serious adverse events	JNJ-56136379-75 mg (Open label)	Placebo (matching JNJ-6379 75 mg) + Nucleos(t)ide analog (NA)	JNJ-56136379- 75 mg + NA
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 28 (3.57%)	0 / 21 (0.00%)	4 / 66 (6.06%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung Adenocarcinoma			

subjects affected / exposed	0 / 28 (0.00%)	0 / 21 (0.00%)	1 / 66 (1.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ligament Rupture			
subjects affected / exposed	0 / 28 (0.00%)	0 / 21 (0.00%)	0 / 66 (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
Post-Traumatic Neck Syndrome			
subjects affected / exposed	0 / 28 (0.00%)	0 / 21 (0.00%)	1 / 66 (1.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac Failure Acute			
subjects affected / exposed	0 / 28 (0.00%)	0 / 21 (0.00%)	1 / 66 (1.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocarditis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 21 (0.00%)	1 / 66 (1.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 21 (0.00%)	1 / 66 (1.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 21 (0.00%)	0 / 66 (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
Reproductive system and breast disorders			
Ovarian Haemorrhage			

subjects affected / exposed	0 / 28 (0.00%)	0 / 21 (0.00%)	0 / 66 (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
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 28 (3.57%)	0 / 21 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral Disc Protrusion			
subjects affected / exposed	0 / 28 (0.00%)	0 / 21 (0.00%)	0 / 66 (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
Muscle Necrosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 21 (0.00%)	1 / 66 (1.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 21 (0.00%)	0 / 66 (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
Toxic Shock Syndrome Streptococcal			
subjects affected / exposed	0 / 28 (0.00%)	0 / 21 (0.00%)	1 / 66 (1.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	JNJ-56136379- 250 mg (Open label)	Placebo (matching to JNJ-56136379 250 mg) + NA	JNJ-56136379- 250 mg + NA
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 32 (0.00%)	1 / 22 (4.55%)	4 / 63 (6.35%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Lung Adenocarcinoma			
subjects affected / exposed	0 / 32 (0.00%)	0 / 22 (0.00%)	0 / 63 (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
Injury, poisoning and procedural complications			
Ligament Rupture			
subjects affected / exposed	0 / 32 (0.00%)	0 / 22 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post-Traumatic Neck Syndrome			
subjects affected / exposed	0 / 32 (0.00%)	0 / 22 (0.00%)	0 / 63 (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
Cardiac disorders			
Cardiac Failure Acute			
subjects affected / exposed	0 / 32 (0.00%)	0 / 22 (0.00%)	0 / 63 (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
Myocarditis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 22 (0.00%)	0 / 63 (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
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 22 (0.00%)	0 / 63 (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
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 32 (0.00%)	1 / 22 (4.55%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian Haemorrhage			

subjects affected / exposed	0 / 32 (0.00%)	0 / 22 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 32 (0.00%)	0 / 22 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral Disc Protrusion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 22 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle Necrosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 22 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 22 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxic Shock Syndrome Streptococcal			
subjects affected / exposed	0 / 32 (0.00%)	0 / 22 (0.00%)	0 / 63 (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	JNJ-56136379-75 mg (Open label)	Placebo (matching JNJ-6379 75 mg) + Nucleos(t)ide analog (NA)	JNJ-56136379- 75 mg + NA
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 28 (64.29%)	13 / 21 (61.90%)	46 / 66 (69.70%)

Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 28 (3.57%)	1 / 21 (4.76%)	2 / 66 (3.03%)
occurrences (all)	1	1	11
Amylase Increased			
subjects affected / exposed	3 / 28 (10.71%)	1 / 21 (4.76%)	1 / 66 (1.52%)
occurrences (all)	6	3	1
Aspartate Aminotransferase Increased			
subjects affected / exposed	1 / 28 (3.57%)	0 / 21 (0.00%)	2 / 66 (3.03%)
occurrences (all)	1	0	7
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	1 / 28 (3.57%)	2 / 21 (9.52%)	4 / 66 (6.06%)
occurrences (all)	1	3	5
Glomerular Filtration Rate Decreased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 21 (0.00%)	3 / 66 (4.55%)
occurrences (all)	0	0	3
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	0 / 28 (0.00%)	0 / 21 (0.00%)	4 / 66 (6.06%)
occurrences (all)	0	0	5
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 28 (3.57%)	0 / 21 (0.00%)	3 / 66 (4.55%)
occurrences (all)	1	0	3
Headache			
subjects affected / exposed	3 / 28 (10.71%)	3 / 21 (14.29%)	11 / 66 (16.67%)
occurrences (all)	4	3	23
General disorders and administration site conditions			
Chest Discomfort			
subjects affected / exposed	0 / 28 (0.00%)	0 / 21 (0.00%)	1 / 66 (1.52%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	2 / 28 (7.14%)	4 / 21 (19.05%)	8 / 66 (12.12%)
occurrences (all)	4	4	8
Influenza Like Illness			

subjects affected / exposed	2 / 28 (7.14%)	1 / 21 (4.76%)	2 / 66 (3.03%)
occurrences (all)	2	1	2
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 28 (3.57%)	2 / 21 (9.52%)	0 / 66 (0.00%)
occurrences (all)	1	2	0
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 28 (0.00%)	1 / 21 (4.76%)	1 / 66 (1.52%)
occurrences (all)	0	2	1
Abdominal Pain Upper			
subjects affected / exposed	1 / 28 (3.57%)	1 / 21 (4.76%)	3 / 66 (4.55%)
occurrences (all)	1	1	3
Constipation			
subjects affected / exposed	2 / 28 (7.14%)	0 / 21 (0.00%)	1 / 66 (1.52%)
occurrences (all)	2	0	1
Diarrhoea			
subjects affected / exposed	2 / 28 (7.14%)	1 / 21 (4.76%)	4 / 66 (6.06%)
occurrences (all)	2	1	4
Nausea			
subjects affected / exposed	2 / 28 (7.14%)	2 / 21 (9.52%)	2 / 66 (3.03%)
occurrences (all)	3	3	2
Toothache			
subjects affected / exposed	0 / 28 (0.00%)	0 / 21 (0.00%)	5 / 66 (7.58%)
occurrences (all)	0	0	5
Hepatobiliary disorders			
Hepatic Pain			
subjects affected / exposed	2 / 28 (7.14%)	0 / 21 (0.00%)	1 / 66 (1.52%)
occurrences (all)	2	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 28 (0.00%)	0 / 21 (0.00%)	2 / 66 (3.03%)
occurrences (all)	0	0	2
Oropharyngeal Pain			
subjects affected / exposed	2 / 28 (7.14%)	1 / 21 (4.76%)	2 / 66 (3.03%)
occurrences (all)	2	1	2

Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	2 / 28 (7.14%)	1 / 21 (4.76%)	1 / 66 (1.52%)
occurrences (all)	2	2	1
Rash			
subjects affected / exposed	0 / 28 (0.00%)	1 / 21 (4.76%)	4 / 66 (6.06%)
occurrences (all)	0	1	4
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 21 (0.00%)	1 / 66 (1.52%)
occurrences (all)	1	0	1
Back Pain			
subjects affected / exposed	2 / 28 (7.14%)	0 / 21 (0.00%)	6 / 66 (9.09%)
occurrences (all)	2	0	6
Musculoskeletal Pain			
subjects affected / exposed	1 / 28 (3.57%)	0 / 21 (0.00%)	1 / 66 (1.52%)
occurrences (all)	1	0	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 21 (0.00%)	0 / 66 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 21 (0.00%)	0 / 66 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 28 (3.57%)	5 / 21 (23.81%)	8 / 66 (12.12%)
occurrences (all)	1	6	10
Pharyngitis			
subjects affected / exposed	1 / 28 (3.57%)	1 / 21 (4.76%)	2 / 66 (3.03%)
occurrences (all)	1	1	2
Rhinitis			
subjects affected / exposed	2 / 28 (7.14%)	0 / 21 (0.00%)	0 / 66 (0.00%)
occurrences (all)	3	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	2 / 28 (7.14%)	0 / 21 (0.00%)	11 / 66 (16.67%)
occurrences (all)	2	0	21

Urinary Tract Infection			
subjects affected / exposed	2 / 28 (7.14%)	0 / 21 (0.00%)	0 / 66 (0.00%)
occurrences (all)	5	0	0
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	1 / 28 (3.57%)	1 / 21 (4.76%)	2 / 66 (3.03%)
occurrences (all)	1	1	2

Non-serious adverse events	JNJ-56136379- 250 mg (Open label)	Placebo (matching to JNJ-56136379 250 mg) + NA	JNJ-56136379- 250 mg + NA
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 32 (71.88%)	14 / 22 (63.64%)	45 / 63 (71.43%)
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	3 / 32 (9.38%)	1 / 22 (4.55%)	6 / 63 (9.52%)
occurrences (all)	3	1	11
Amylase Increased			
subjects affected / exposed	1 / 32 (3.13%)	0 / 22 (0.00%)	3 / 63 (4.76%)
occurrences (all)	4	0	7
Aspartate Aminotransferase Increased			
subjects affected / exposed	1 / 32 (3.13%)	1 / 22 (4.55%)	4 / 63 (6.35%)
occurrences (all)	1	1	7
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	1 / 32 (3.13%)	1 / 22 (4.55%)	1 / 63 (1.59%)
occurrences (all)	1	1	1
Glomerular Filtration Rate Decreased			
subjects affected / exposed	3 / 32 (9.38%)	0 / 22 (0.00%)	1 / 63 (1.59%)
occurrences (all)	3	0	1
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	0 / 32 (0.00%)	0 / 22 (0.00%)	1 / 63 (1.59%)
occurrences (all)	0	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 32 (12.50%)	0 / 22 (0.00%)	2 / 63 (3.17%)
occurrences (all)	6	0	2
Headache			

subjects affected / exposed	7 / 32 (21.88%)	1 / 22 (4.55%)	14 / 63 (22.22%)
occurrences (all)	8	1	22
General disorders and administration site conditions			
Chest Discomfort			
subjects affected / exposed	2 / 32 (6.25%)	0 / 22 (0.00%)	0 / 63 (0.00%)
occurrences (all)	2	0	0
Fatigue			
subjects affected / exposed	2 / 32 (6.25%)	0 / 22 (0.00%)	5 / 63 (7.94%)
occurrences (all)	2	0	7
Influenza Like Illness			
subjects affected / exposed	0 / 32 (0.00%)	0 / 22 (0.00%)	0 / 63 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 32 (0.00%)	1 / 22 (4.55%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	1 / 32 (3.13%)	0 / 22 (0.00%)	5 / 63 (7.94%)
occurrences (all)	1	0	5
Abdominal Pain Upper			
subjects affected / exposed	2 / 32 (6.25%)	0 / 22 (0.00%)	5 / 63 (7.94%)
occurrences (all)	2	0	7
Constipation			
subjects affected / exposed	3 / 32 (9.38%)	0 / 22 (0.00%)	1 / 63 (1.59%)
occurrences (all)	3	0	2
Diarrhoea			
subjects affected / exposed	1 / 32 (3.13%)	0 / 22 (0.00%)	5 / 63 (7.94%)
occurrences (all)	1	0	6
Nausea			
subjects affected / exposed	2 / 32 (6.25%)	1 / 22 (4.55%)	5 / 63 (7.94%)
occurrences (all)	2	1	6
Toothache			
subjects affected / exposed	1 / 32 (3.13%)	0 / 22 (0.00%)	2 / 63 (3.17%)
occurrences (all)	2	0	2
Hepatobiliary disorders			

Hepatic Pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 22 (0.00%)	0 / 63 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 32 (9.38%)	1 / 22 (4.55%)	2 / 63 (3.17%)
occurrences (all)	3	1	2
Oropharyngeal Pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 22 (0.00%)	4 / 63 (6.35%)
occurrences (all)	0	0	6
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 32 (0.00%)	0 / 22 (0.00%)	5 / 63 (7.94%)
occurrences (all)	0	0	9
Rash			
subjects affected / exposed	4 / 32 (12.50%)	0 / 22 (0.00%)	2 / 63 (3.17%)
occurrences (all)	4	0	7
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 22 (0.00%)	5 / 63 (7.94%)
occurrences (all)	0	0	5
Back Pain			
subjects affected / exposed	3 / 32 (9.38%)	1 / 22 (4.55%)	3 / 63 (4.76%)
occurrences (all)	3	1	3
Musculoskeletal Pain			
subjects affected / exposed	3 / 32 (9.38%)	1 / 22 (4.55%)	0 / 63 (0.00%)
occurrences (all)	3	1	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 32 (0.00%)	2 / 22 (9.09%)	2 / 63 (3.17%)
occurrences (all)	0	2	2
Gastroenteritis			
subjects affected / exposed	2 / 32 (6.25%)	0 / 22 (0.00%)	2 / 63 (3.17%)
occurrences (all)	2	0	4
Nasopharyngitis			

subjects affected / exposed	4 / 32 (12.50%)	4 / 22 (18.18%)	10 / 63 (15.87%)
occurrences (all)	6	5	10
Pharyngitis			
subjects affected / exposed	2 / 32 (6.25%)	1 / 22 (4.55%)	1 / 63 (1.59%)
occurrences (all)	2	1	1
Rhinitis			
subjects affected / exposed	2 / 32 (6.25%)	0 / 22 (0.00%)	1 / 63 (1.59%)
occurrences (all)	2	0	2
Upper Respiratory Tract Infection			
subjects affected / exposed	5 / 32 (15.63%)	2 / 22 (9.09%)	4 / 63 (6.35%)
occurrences (all)	6	3	8
Urinary Tract Infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 22 (0.00%)	0 / 63 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	1 / 32 (3.13%)	0 / 22 (0.00%)	4 / 63 (6.35%)
occurrences (all)	1	0	6

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 December 2017	The overall reason for Amendment 1, considered a substantial protocol amendment and issued on 18 December 2017, was to incorporate Health Authority feedback regarding follow-up treatment and safety monitoring after the 24-week treatment period and hormonal contraceptive treatment.
06 March 2018	The overall reason for Amendment 2, considered a substantial protocol amendment and issued on 6 March 2018, was to implement the Health Authority recommendation to evaluate the effect of extended treatment on hepatitis B surface antigen (HBsAg) decline.
20 February 2019	The overall reasons for Amendment 4, considered a substantial protocol amendment and issued on 20 February 2019, were to implement an urgent safety measure based on DRC recommendations and also include a futility rule.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported