Clinical trial results:
Phase IIb, Double-Blinded, Multicenter, Randomized Study to Assess the Effect on Central Nervous System (CNS) Toxicity of Switching from ATRIPLA™ (Efavirenz, Tenofovir, Emtricitabine) to MK-1439A (Doravirine, Tenofovir, Lamivudine) in Virologically-Suppressed Subjects

Summary

EudraCT number	2015-003617-18
Trial protocol	GB IE
Global end of trial date	07 February 2024

Results information

Result version number	v1 (current)
This version publication date	09 February 2025
First version publication date	09 February 2025

Trial information

Trial identification

Sponsor protocol code	MK-1439A-028

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02652260
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme LLC
Sponsor organisation address	126 East Lincoln Avenue, P.O. Box 2000, Rahway, NJ, United States, 07065
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@msd.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@msd.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	07 February 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 August 2018
Global end of trial reached?	Yes
Global end of trial date	07 February 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study aims to evaluate a switch from fixed dose combination (FDC) treatment with ATRIPLA^TM for 12 weeks prior to screening to FDC treatment with Doravirine, Tenofovir, Lamivudine (MK-1439A) in virologically-suppressed, human immunodeficiency virus type 1 (HIV-1)-infected participants. The primary hypothesis is that switching from ATRIPLA^TM to Doravirine, Tenofovir, Lamivudine results in a lower proportion of participants with at least one CNS toxicity of at least Grade 2 intensity at Week 12 than continuation of ATRIPLA^TM treatment.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 March 2016
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	Ireland: 2
Country: Number of subjects enrolled	South Africa: 45
Country: Number of subjects enrolled	United Kingdom: 39
Worldwide total number of subjects	86
EEA total number of subjects	2

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)	82
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Out of 112 participants screened, 86 were randomized and received study treatment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Immediate Switch to MK-1439A

Arm description:

Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening will be switched to blinded MK-1439A orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for an additional 12 weeks. Eligible participants from Base Study (Day 1 to Week 24) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 24 to 120), Extension 2 (Weeks 120 to 216), and Extension 3 (Weeks 216 to 312).

Arm type	Experimental
Investigational medicinal product name	Doravirine, Tenofovir, Lamivudine
Investigational medicinal product code	
Other name	MK-1439A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A single tablet FDC containing doravirine 100 mg, lamivudine (3TC) 300 mg and tenofovir disoproxil fumarate (TDF) 300 mg administered orally, once daily for 12 weeks during the Blinded period and 12 weeks during the Open-Label period.

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

Dosage and administration details:

A single placebo to ATRIPLA™ tablet administered orally, once daily for 12 weeks during the Blinded period.

Investigational medicinal product name	Placebo to Doravirine, Tenofovir, Lamivudine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A single placebo to doravirine, tenofovir, lamivudine tablet administered orally, once daily for 12 weeks during the Blinded period.

Arm title	Deferred Switch to MK-1439A

Arm description:

Participants continued their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks (Day 1 to Week

12), followed by open-label MK-1439A orally, once daily for 24 weeks (Weeks 12 to 36). Eligible participants from Base Study (Day 1 to Week 36) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 36 to 132), Extension 2 (Weeks 132 to 228), and Extension 3 (Weeks 228 to 324).

Arm type	Active comparator
Investigational medicinal product name	ATRIPLA™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A single tablet FDC containing efavirenz (EFV) 600 mg, emtricitabine (FTC) 200 mg, and TDF 300 mg administered orally, once daily for 12 weeks during the Blinded period.

Investigational medicinal product name	Doravirine, Tenofovir, Lamivudine
Investigational medicinal product code	
Other name	MK-1439A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A single-tablet FDC containing doravirine 100 mg, 3TC 300 mg and TDF 300 mg administered orally, once daily for 24 weeks during the Open-Label period.

Number of subjects in period 1	Immediate Switch to MK-1439A	Deferred Switch to MK-1439A
Started	43	43
Switched Over to MK-1439A	0 [1]	42
Completed	43	41
Not completed	0	2
Consent withdrawn by subject	-	1
Pregnancy	-	1

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Only participants in the Deferred Switch to MK-1439A arm switched treatments.

Period 2

Period 2 title	Study Extension 1 (Open-Label)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Immediate Switch to MK-1439A

Arm description:

Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening will be switched to blinded MK-1439A orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for an additional 12 weeks. Eligible participants from Base Study (Day 1 to Week 24) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 24 to 120), Extension 2 (Weeks 120 to 216), and Extension 3 (Weeks 216 to 312).

Arm type	Experimental
Investigational medicinal product name	Doravirine, Tenofovir, Lamivudine
Investigational medicinal product code	
Other name	MK-1439A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A single-tablet FDC containing doravirine 100 mg, 3TC 300 mg and TDF 300 mg administered orally, once daily for an additional 96 weeks during the Open-Label extension period 1.

Arm title	Deferred Switch to MK-1439A

Arm description:

Participants continued their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks (Day 1 to Week 12), followed by open-label MK-1439A orally, once daily for 24 weeks (Weeks 12 to 36). Eligible participants from Base Study (Day 1 to Week 36) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 36 to 132), Extension 2 (Weeks 132 to 228), and Extension 3 (Weeks 228 to 324).

Arm type	Active comparator
Investigational medicinal product name	Doravirine, Tenofovir, Lamivudine
Investigational medicinal product code	
Other name	MK-1439A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A single-tablet FDC containing doravirine 100 mg, 3TC 300 mg and TDF 300 mg administered orally, once daily for an additional 96 weeks during the Open-Label extension period 1.

Number of subjects in period 2	Immediate Switch to MK-1439A	Deferred Switch to MK-1439A
Started	43	41
Completed	39	34
Not completed	4	7
Consent withdrawn by subject	1	2
Availability of study drug locally	1	1
Adverse event, non-fatal	-	2
Pregnancy	1	1
Lack of efficacy	1	1

Period 3

Period 3 title	Study Extension 2 (Open-Label)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes

Arm title	Immediate Switch to MK-1439A

Arm description:

Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening will be switched to blinded MK-1439A orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for an additional 12 weeks. Eligible participants from Base Study (Day 1 to Week 24) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 24 to 120), Extension 2 (Weeks 120 to 216), and Extension 3 (Weeks 216 to 312).

Arm type	Experimental
Investigational medicinal product name	Doravirine, Tenofovir, Lamivudine
Investigational medicinal product code	
Other name	MK-1439A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A single-tablet FDC containing doravirine 100 mg, 3TC 300 mg and TDF 300 mg administered orally, once daily for a maximum total duration of treatment of 228 weeks during the Open-Label extension period 2.

Arm title	Deferred Switch to MK-1439A

Arm description:

Participants continued their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks (Day 1 to Week 12), followed by open-label MK-1439A orally, once daily for 24 weeks (Weeks 12 to 36). Eligible participants from Base Study (Day 1 to Week 36) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 36 to 132), Extension 2 (Weeks 132 to 228), and Extension 3 (Weeks 228 to 324).

Arm type	Active comparator
Investigational medicinal product name	Doravirine, Tenofovir, Lamivudine
Investigational medicinal product code	
Other name	MK-1439A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A single-tablet FDC containing doravirine 100 mg, 3TC 300 mg and TDF 300 mg administered orally, once daily for a maximum total duration of treatment of 228 weeks during the Open-Label extension period 2.

Number of subjects in period 3[2]	Immediate Switch to MK-1439A	Deferred Switch to MK-1439A
Started	39	33
Completed	17	19
Not completed	22	14
Adverse event, non-fatal	1	-
Availability of study drug locally	18	13
Pregnancy	1	1
Non-Compliance with study drug	1	-
Lost to follow-up	1	-

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all study participants continued into optional study extension 2.

Period 4

Period 4 title	Study Extension 3 (Open-Label)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Immediate Switch to MK-1439A

Arm description:

Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening will be switched to blinded MK-1439A orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for an additional 12 weeks. Eligible participants from Base Study (Day 1 to Week 24) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 24 to 120), Extension 2 (Weeks 120 to 216), and Extension 3 (Weeks 216 to 312).

Arm type	Experimental
Investigational medicinal product name	Doravirine, Tenofovir, Lamivudine
Investigational medicinal product code	
Other name	MK-1439A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A single-tablet FDC containing doravirine 100 mg, 3TC 300 mg and TDF 300 mg administered orally, once daily for a maximum total duration of treatment of 324 weeks during the Open-Label extension period 3.

Arm title	Deferred Switch to MK-1439A

Arm description:

Participants continued their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks (Day 1 to Week 12), followed by open-label MK-1439A orally, once daily for 24 weeks (Weeks 12 to 36). Eligible participants from Base Study (Day 1 to Week 36) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 36 to 132), Extension 2 (Weeks 132 to 228), and Extension 3 (Weeks 228 to 324).

Arm type	Active comparator
Investigational medicinal product name	Doravirine, Tenofovir, Lamivudine
Investigational medicinal product code	
Other name	MK-1439A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A single-tablet FDC containing doravirine 100 mg, 3TC 300 mg and TDF 300 mg administered orally, once daily for a maximum total duration of treatment of 324 weeks during the Open-Label extension period 3

Number of subjects in period 4	Immediate Switch to MK-1439A	Deferred Switch to MK-1439A
Started	17	19
Completed	10	8
Not completed	7	11
Physician decision	7	10
Pregnancy	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Immediate Switch to MK-1439A
Reporting group description:	
Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening will be switched to blinded MK-1439A orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for an additional 12 weeks. Eligible participants from Base Study (Day 1 to Week 24) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 24 to 120), Extension 2 (Weeks 120 to 216), and Extension 3 (Weeks 216 to 312).	
Reporting group title	Deferred Switch to MK-1439A
Reporting group description:	
Participants continued their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks (Day 1 to Week 12), followed by open-label MK-1439A orally, once daily for 24 weeks (Weeks 12 to 36). Eligible participants from Base Study (Day 1 to Week 36) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 36 to 132), Extension 2 (Weeks 132 to 228), and Extension 3 (Weeks 228 to 324).	

Reporting group values	Immediate Switch to MK-1439A	Deferred Switch to MK-1439A	Total
Number of subjects	43	43	86
Age categorical Units: Participants			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	40	42	82
From 65-84 years	3	1	4
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	41.8	41.6	
standard deviation	± 11.9	± 11.2	-
Sex: Female, Male Units: Participants			
Female	19	17	36
Male	24	26	50
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	3	1	4
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	25	23	48
White	12	19	31
More than one race	3	0	3
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB)			

Units: Subjects			
Hispanic or Latino	4	1	5
Not Hispanic or Latino	39	42	81
Unknown or Not Reported	0	0	0
CNS Toxicity Percentage Of Maximum Score			
Participants were asked to rate the intensity for each of the 10 events as none (Grade 0), mild (Grade 1), moderate (Grade 2), or severe (Grade 3). Mild = symptom is noticeable but does not interfere with normal activities; moderate = symptom has some impact on normal activities; severe = symptom prevents conduct of normal activities. The CNS toxicity score was calculated by summing across all 10 CNS toxicities and converting the sum to a percentage of the maximum possible sum of intensities (10 x 3 = 30). A higher CNS score indicates worsening symptoms.			
Units: Percentage of maximum score			
arithmetic mean	32.9	37.1	
standard deviation	± 16.5	± 19.0	-
Fasting Lipids - LDL Cholesterol			
Mean concentrations of low-density lipoprotein (LDL) cholesterol. All randomized participants who received at least one dose of study treatment were analyzed.			
Units: mg/dL			
arithmetic mean	98.67	99.54	
standard deviation	± 35.28	± 33.57	-
Fasting Lipids - Non-HDL Cholesterol			
Mean concentrations of non high-density lipoprotein (HDL) cholesterol. All randomized participants who received at least one dose of study treatment were analyzed			
Units: mg/dL			
arithmetic mean	118.73	117.76	
standard deviation	± 36.93	± 37.83	-
Fasting Lipids - Cholesterol			
Mean concentrations of cholesterol. All randomized participants who received at least one dose of study treatment were analyzed.			
Units: mg/dL			
arithmetic mean	178.11	173.02	
standard deviation	± 36.39	± 36.62	-
Fasting Lipids - HDL Cholesterol			
Mean concentrations of HDL cholesterol. All randomized participants who received at least one dose of study treatment.			
Units: mg/dL			
arithmetic mean	59.38	55.27	
standard deviation	± 14.58	± 14.00	-
Fasting Lipids - Triglyceride			
Mean concentrations of triglyceride. All randomized participants who received at least one dose of study treatment.			
Units: mg/dL			
arithmetic mean	107.49	91.39	
standard deviation	± 65.64	± 39.43	-

End points reporting groups

Reporting group title	Immediate Switch to MK-1439A

Reporting group description:

Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening will be switched to blinded MK-1439A orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for an additional 12 weeks. Eligible participants from Base Study (Day 1 to Week 24) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 24 to 120), Extension 2 (Weeks 120 to 216), and Extension 3 (Weeks 216 to 312).

Reporting group title	Deferred Switch to MK-1439A

Reporting group description:

Participants continued their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks (Day 1 to Week 12), followed by open-label MK-1439A orally, once daily for 24 weeks (Weeks 12 to 36). Eligible participants from Base Study (Day 1 to Week 36) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 36 to 132), Extension 2 (Weeks 132 to 228), and Extension 3 (Weeks 228 to 324).

Reporting group title	Immediate Switch to MK-1439A

Reporting group description:

Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening will be switched to blinded MK-1439A orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for an additional 12 weeks. Eligible participants from Base Study (Day 1 to Week 24) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 24 to 120), Extension 2 (Weeks 120 to 216), and Extension 3 (Weeks 216 to 312).

Reporting group title	Deferred Switch to MK-1439A

Reporting group description:

Participants continued their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks (Day 1 to Week 12), followed by open-label MK-1439A orally, once daily for 24 weeks (Weeks 12 to 36). Eligible participants from Base Study (Day 1 to Week 36) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 36 to 132), Extension 2 (Weeks 132 to 228), and Extension 3 (Weeks 228 to 324).

Reporting group title	Immediate Switch to MK-1439A

Reporting group description:

Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening will be switched to blinded MK-1439A orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for an additional 12 weeks. Eligible participants from Base Study (Day 1 to Week 24) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 24 to 120), Extension 2 (Weeks 120 to 216), and Extension 3 (Weeks 216 to 312).

Reporting group title	Deferred Switch to MK-1439A

Reporting group description:

Participants continued their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks (Day 1 to Week 12), followed by open-label MK-1439A orally, once daily for 24 weeks (Weeks 12 to 36). Eligible participants from Base Study (Day 1 to Week 36) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 36 to 132), Extension 2 (Weeks 132 to 228), and Extension 3 (Weeks 228 to 324).

Reporting group title	Immediate Switch to MK-1439A

Reporting group description:

Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening will be switched to blinded MK-1439A orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for an additional 12 weeks. Eligible participants from Base Study (Day 1 to Week 24) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 24 to 120), Extension 2 (Weeks 120 to 216), and Extension 3 (Weeks 216 to 312).

Reporting group title	Deferred Switch to MK-1439A

Reporting group description:

Participants continued their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks (Day 1 to Week 12), followed by open-label MK-1439A orally, once daily for 24 weeks (Weeks 12 to 36). Eligible participants from Base Study (Day 1 to Week 36) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 36 to 132), Extension 2 (Weeks 132 to 228), and Extension 3 (Weeks 228 to 324).

Subject analysis set title	Combined Treatment Groups: Time of Switch
Subject analysis set type	Per protocol

Subject analysis set description:

Immediate Switch to MK-1439A: Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening will be switched to blinded MK-1439A orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for an additional 12 weeks.
Deferred Switch to MK-1439A: Participants will continue on their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for 24 weeks.

Subject analysis set title	Combined Treatment Groups: Week 24 Post-Switch
Subject analysis set type	Per protocol

Subject analysis set description:

Immediate Switch to MK-1439A: Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening will be switched to blinded MK-1439A orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for an additional 12 weeks.
Deferred Switch to MK-1439A: Participants will continue on their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for 24 weeks.

Subject analysis set title	Combined Treatment Groups
Subject analysis set type	Per protocol

Subject analysis set description:

Immediate Switch to MK-1439A: Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening will be switched to blinded MK-1439A orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for an additional 12 weeks.
Deferred Switch to MK-1439A: Participants will continue on their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for 24 weeks.

Subject analysis set title	Combined Treatment Groups
Subject analysis set type	Per protocol

Subject analysis set description:

Immediate Switch to MK-1439A: Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening will be switched to blinded MK-1439A orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for an additional 12 weeks.
Deferred Switch to MK-1439A: Participants will continue on their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for 24 weeks.

Primary: Percentage of participants with at least one central nervous system (CNS) toxicity of at least grade 2 intensity at week 12

End point title	Percentage of participants with at least one central nervous system (CNS) toxicity of at least grade 2 intensity at week 12

End point description:

A questionnaire was used to solicit for CNS toxicity based on the following 10 events: dizziness; depression/low mood; insomnia/sleeplessness; anxiety/nervousness; confusion; impaired concentration/attention; headache; somnolence/daytime sleepiness; aggressive mood/behavior; and abnormal dreams. Participants were asked to rate the intensity for each of the 10 events as none (Grade 0), mild (Grade 1), moderate (Grade 2), or severe (Grade 3). Mild = symptom is noticeable but does not interfere with normal activities; moderate = symptom has some impact on normal activities; severe = symptom prevents conduct of normal activities. Percentage of participants with at least one CNS toxicity of Grade 2 or higher were recorded, based on the last observation carried forward (LOCF) approach. All randomized participants who received at least one dose of study treatment, and have baseline data for analyses requiring baseline data were analyzed.

End point type	Primary

End point timeframe:

Week 12

End point values	Immediate Switch to MK-1439A	Deferred Switch to MK-1439A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	43		
Units: Percentage of participants				
number (not applicable)	41.9	37.2		

Statistical analyses

Statistical analysis title	Treatment Difference: Immediate - Delayed Switch

Statistical analysis description:

The Immediate Switch group will be considered statistically significantly smaller than the Delayed Switch group if the upper bound of the 95% confidence interval for the treatment difference is less than 0.

Comparison groups	Immediate Switch to MK-1439A v Deferred Switch to MK-1439A
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.331
Method	Miettinen and Nurminen
Parameter estimate	Estimated Difference
Point estimate	4.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.92
upper limit	24.85

Secondary: Percentage of participants with at least one CNS toxicity of at least grade 2 intensity at week 4

End point title	Percentage of participants with at least one CNS toxicity of at least grade 2 intensity at week 4

End point description:

A questionnaire was used to solicit for CNS toxicity based on the following 10 events: dizziness; depression/low mood; insomnia/sleeplessness; anxiety/nervousness; confusion; impaired concentration/attention; headache; somnolence/daytime sleepiness; aggressive mood/behavior; and abnormal dreams. Participants were asked to rate the intensity for each of the 10 events as none (Grade 0), mild (Grade 1), moderate (Grade 2), or severe (Grade 3). Mild = symptom is noticeable but does not interfere with normal activities; moderate = symptom has some impact on normal activities; severe = symptom prevents conduct of normal activities. Percentage of participants with at least one CNS toxicity of Grade 2 or higher were recorded, based on the last observation carried forward (LOCF) approach. All randomized participants who received at least one dose of study treatment, and have baseline data for analyses requiring baseline data were analyzed.

End point type	Secondary

End point timeframe:

Week 4

End point values	Immediate Switch to MK-1439A	Deferred Switch to MK-1439A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	43		
Units: Percentage of participants				
number (not applicable)	46.5	65.1		

Statistical analyses

Statistical analysis title	Treatment Difference: Immediate - Delayed Switch

Statistical analysis description:

The Immediate Switch group will be considered statistically significantly smaller than the Delayed Switch group if the upper bound of the 95% confidence interval for the treatment difference is less than 0.

Comparison groups	Immediate Switch to MK-1439A v Deferred Switch to MK-1439A
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Estimated Difference
Point estimate	-18.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-38.14
upper limit	2.51

Secondary: Change from baseline in CNS toxicity score at week 4

End point title	Change from baseline in CNS toxicity score at week 4

End point description:

A questionnaire was used to solicit for CNS toxicity based on 10 events: dizziness; depression/low mood; insomnia/sleeplessness; anxiety/nervousness; confusion; impaired concentration/attention; headache; somnolence/daytime sleepiness; aggressive mood/behavior; & abnormal dreams. Participants were asked to rate the intensity of the 10 events as none (Grade 0), mild (Grade 1), moderate (Grade 2), or severe (Grade 3). Mild = symptom is noticeable but does not interfere with normal activities; moderate = symptom has some impact on normal activities; severe = symptom prevents conduct of normal activities. The CNS toxicity score was calculated by summing all 10 CNS toxicities & converting to a percentage of the maximum possible sum of intensities. A positive change from baseline score = worsening symptoms. A negative change from baseline score = improvement in symptoms. All randomized participants who received ≥1 dose of study treatment & had baseline data where applicable were analyzed.

End point type	Secondary

End point timeframe:

Baseline and Week 4

End point values	Immediate Switch to MK-1439A	Deferred Switch to MK-1439A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	43		
Units: Percentage of maximum score				
arithmetic mean (confidence interval 95%)	-17.6 (-23.4 to -11.8)	-15.6 (-22.0 to -9.2)		

Statistical analyses

Statistical analysis title	Treatment Difference: Immediate - Delayed Switch
Comparison groups	Immediate Switch to MK-1439A v Deferred Switch to MK-1439A
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Estimated Difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.5
upper limit	6.5

Secondary: Percentage of participants with at least one CNS toxicity of at least grade 2 intensity at time of switch, and at 24 weeks post-switch for the combined treatment groups

End point title	Percentage of participants with at least one CNS toxicity of at least grade 2 intensity at time of switch, and at 24 weeks post-switch for the combined treatment groups

End point description:

A questionnaire was used to solicit for CNS toxicity based on 10 events: dizziness; depression/low mood; insomnia/sleeplessness; anxiety/nervousness; confusion; impaired concentration/attention; headache; somnolence/daytime sleepiness; aggressive mood/behavior; & abnormal dreams. Participants were asked to rate the intensity for the 10 events as none (Grade 0), mild (Grade 1), moderate (Grade 2), or severe (Grade 3). Mild = symptom is noticeable but does not interfere with normal activities; moderate = symptom has some impact on normal activities; severe = symptom prevents conduct of normal activities. For the Immediate Switch Group (ISG) time of switch was study Day 1, and week 24 post-switch was week 24. For the Delayed Switch Group (DSG) time of switch was study week 12, and week 24 post-switch was week 36. All randomized participants who received at least one dose of study treatment & had baseline data when applicable. Per protocol, the combined treatment groups were analyzed.

End point type	Secondary

End point timeframe:

Baseline (time of switch) and 24 weeks post-switch

End point values	Combined Treatment Groups: Time of Switch	Combined Treatment Groups: Week 24 Post-Switch		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	86	86		
Units: Percentage of participants				
number (not applicable)	68.6	30.2		

Statistical analyses

Statistical analysis title	Treatment Difference: Immediate - Delayed Switch
Statistical analysis description:	
Change from time of switch to 24 weeks post-switch: Treatment difference in percent response	
Comparison groups	Combined Treatment Groups: Week 24 Post-Switch v Combined Treatment Groups: Time of Switch
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in Percentage
Point estimate	-38.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-51.2
upper limit	-23.8

Secondary: Change from baseline in CNS toxicity score at week 12

End point title	Change from baseline in CNS toxicity score at week 12

End point description:

A questionnaire was used to solicit for CNS toxicity based on 10 events: dizziness; depression/low mood; insomnia/sleeplessness; anxiety/nervousness; confusion; impaired concentration/attention; headache; somnolence/daytime sleepiness; aggressive mood/behavior; & abnormal dreams. Participants were asked to rate the intensity of the 10 events as none (Grade 0), mild (Grade 1), moderate (Grade 2), or severe (Grade 3). Mild = symptom is noticeable but does not interfere with normal activities; moderate = symptom has some impact on normal activities; severe = symptom prevents conduct of normal activities. The CNS toxicity score was calculated by summing all 10 CNS toxicities & converting to a percentage of the maximum possible sum of intensities. A positive change from baseline score = worsening symptoms. A negative change from baseline score = improvement in symptoms. All randomized participants who received ≥1 dose of study treatment & had baseline data where applicable were analyzed.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Immediate Switch to MK-1439A	Deferred Switch to MK-1439A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	43		
Units: Percentage of maximum score				
arithmetic mean (confidence interval 95%)	-18.1 (-22.9 to -13.3)	-21.7 (-27.9 to -15.5)		

Statistical analyses

Statistical analysis title	Treatment Difference: Immediate - Delayed Switch
Comparison groups	Immediate Switch to MK-1439A v Deferred Switch to MK-1439A
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Estimated Difference
Point estimate	3.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.1
upper limit	11.3

Secondary: Change from baseline in fasting lipids at week 12

End point title	Change from baseline in fasting lipids at week 12

End point description:

Blood was collected under fasting conditions on Day 1 and on week 12 in order to determine the concentration of the following lipids: low-density lipoprotein (LDL) cholesterol; Non high-density lipoprotein (HDL) cholesterol; cholesterol; HDL cholesterol; and triglyceride. All randomized participants who received at least one dose of study treatment, and have required lipid data were analyzed.

End point type	Secondary

End point timeframe:

Baseline (study Day 1) and study week 12

End point values	Immediate Switch to MK-1439A	Deferred Switch to MK-1439A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	41		
Units: mg/dL				
arithmetic mean (standard deviation)				
LDL Cholesterol	-10.78 (± 15.85)	-1.88 (± 14.88)		
Non-HDL Cholesterol	-14.08 (± 17.17)	-0.37 (± 16.51)		

Cholesterol	-22.14 (± 19.49)	0.00 (± 18.04)		
HDL Cholesterol	-8.05 (± 7.74)	0.37 (± 7.91)		
Triglyceride	-21.19 (± 43.37)	7.10 (± 38.55)		

Statistical analyses

Statistical analysis title	Difference Estimate: LDL Cholesterol
Statistical analysis description:	
The 95% CI for treatment difference was calculated from an ANCOVA model with terms for baseline lipid level, use of lipid lowering therapy at study Day 1 and treatment	
Comparison groups	Immediate Switch to MK-1439A v Deferred Switch to MK-1439A
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference Estimate
Point estimate	-9.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.69
upper limit	-2.35

Statistical analysis title	Difference Estimate: Non-HDL Cholesterol
Statistical analysis description:	
The 95% CI for treatment difference was calculated from an ANCOVA model with terms for baseline lipid level, use of lipid lowering therapy at study Day 1 and treatment	
Comparison groups	Immediate Switch to MK-1439A v Deferred Switch to MK-1439A
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference Estimate
Point estimate	-13.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.79
upper limit	-6.35

Statistical analysis title	Difference Estimate: Triglyceride
Statistical analysis description:	
The 95% CI for treatment difference was calculated from an ANCOVA model with terms for baseline lipid level, use of lipid lowering therapy at study Day 1 and treatment	

Comparison groups	Immediate Switch to MK-1439A v Deferred Switch to MK-1439A
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference Estimate
Point estimate	-22.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-38.52
upper limit	-5.84

Statistical analysis title	Difference Estimate: HDL Cholesterol

Statistical analysis description:

The 95% CI for treatment difference was calculated from an ANCOVA model with terms for baseline lipid level, use of lipid lowering therapy at study Day 1 and treatment

Comparison groups	Immediate Switch to MK-1439A v Deferred Switch to MK-1439A
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference Estimate
Point estimate	-8.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.76
upper limit	-4.6

Statistical analysis title	Difference Estimate: Cholesterol

Statistical analysis description:

The 95% CI for treatment difference was calculated from an ANCOVA model with terms for baseline lipid level, use of lipid lowering therapy at study Day 1 and treatment

Comparison groups	Immediate Switch to MK-1439A v Deferred Switch to MK-1439A
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference Estimate
Point estimate	-21.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.63
upper limit	-13.21

Secondary: CNS toxicity scores at time of switch, and at 24 weeks post-switch for the combined treatment groups

End point title	CNS toxicity scores at time of switch, and at 24 weeks post-switch for the combined treatment groups

End point description:

A questionnaire was used to solicit for CNS toxicity based on 10 events: dizziness; depression/low mood; insomnia/sleeplessness; anxiety/nervousness; confusion; impaired concentration/attention; headache; somnolence/daytime sleepiness; aggressive mood/behavior; & abnormal dreams. Participants were asked to rate the intensity for the 10 events as none (Grade 0) through severe (Grade 3). The CNS toxicity score was calculated by summing across all 10 CNS toxicities and converted to a percentage of the maximum possible sum of intensities. A higher CNS score = worse symptoms. A positive change in CNS score = worsening symptoms. A negative change = improvement in symptoms. For the ISG time of switch was Day 1, and week 24 post-switch was week 24. For the DSG time of switch was week 12, and week 24 post-switch was week 36. All randomized participants who received ≥1 dose of study treatment & had baseline data where applicable. Per protocol, the combined treatment groups were analyzed.

End point type	Secondary

End point timeframe:

Baseline (time of switch) and 24 weeks post-switch

End point values	Combined Treatment Groups: Time of Switch	Combined Treatment Groups: Week 24 Post-Switch		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	86	86		
Units: Percentage of maximum score				
arithmetic mean (confidence interval 95%)	24.2 (20.5 to 27.9)	10.7 (8.7 to 12.8)		

Statistical analyses

Statistical analysis title	Treatment Difference: Immediate - Delayed Switch

Statistical analysis description:

Change from time of switch to 24 weeks post-switch: Treatment difference in score

Comparison groups	Combined Treatment Groups: Time of Switch v Combined Treatment Groups: Week 24 Post-Switch
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	-13.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.8
upper limit	-10.1

Secondary: Change in fasting lipids between time of switch and week 24 post-switch for the combined treatment groups

End point title	Change in fasting lipids between time of switch and week 24 post-switch for the combined treatment groups

End point description:

Blood was collected under fasting conditions at time of switch and 24 weeks post-switch in order to determine the change from baseline of the following lipids: low-density lipoprotein (LDL) cholesterol; Non high-density lipoprotein (HDL) cholesterol; cholesterol; HDL cholesterol; and triglyceride. For the ISG time of switch was study Day 1, and week 24 post-switch was week 24. For the DSG time of switch was study week 12, and week 24 post-switch was week 36. All randomized participants who received at least one dose of study treatment, and have required lipid data. Based on the protocol-specified plan, the combined treatment groups was analyzed.

End point type	Secondary

End point timeframe:

Baseline (time of switch) and 24 weeks post-switch

End point values	Combined Treatment Groups			
Subject group type	Subject analysis set			
Number of subjects analysed	76			
Units: mg/dL				
arithmetic mean (standard deviation)				
LDL Cholesterol	-10.97 (± 17.15)			
Non-HDL Cholesterol	-13.18 (± 19.82)			
Cholesterol	-20.91 (± 20.19)			
HDL Cholesterol	-7.72 (± 9.53)			
Triglyceride	-12.99 (± 46.61)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with HIV-1 RNA <50 and <40 copies/ml at week 24 post-switch for the combined treatment groups

End point title	Percentage of participants with HIV-1 RNA <50 and <40 copies/ml at week 24 post-switch for the combined treatment groups

End point description:

Blood was collected under fasting conditions at 24 weeks post-switch in order to determine the HIV-1 RNA. For the ISG week 24 post-switch was week 24. For the DSG week 24 post-switch was week 36. All randomized participants who received at least one dose of study treatment, and have required HIV-1 RNA data. Based on the protocol-specified plan, the combined treatment groups was analyzed.

End point type	Secondary

End point timeframe:

24 weeks post-switch

End point values	Combined Treatment Groups			
Subject group type	Subject analysis set			
Number of subjects analysed	85			
Units: Percentage of participants				
number (confidence interval 95%)				
< 50 copies/mL	95.3 (88.4 to 98.7)			
< 40 copies/mL	95.3 (88.4 to 98.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from time of switch to week 24 post switch in CD4 T-cell count for the combined treatment groups

End point title	Change from time of switch to week 24 post switch in CD4 T-cell count for the combined treatment groups

End point description:

Blood was collected at time of switch and at 24 weeks post-switch in order to determine the CD4 T-cell count. For the ISG time of switch was study Day 1, and week 24 post-switch was week 24. For the DSG time of switch was study week 12, and week 24 post-switch was week 36. All randomized participants who received at least one dose of study treatment, and have required CD4 T-cell data. Based on the protocol-specified plan, the combined treatment groups was analyzed.

End point type	Secondary

End point timeframe:

Baseline (time of switch) and 24 weeks post-switch

End point values	Combined Treatment Groups			
Subject group type	Subject analysis set			
Number of subjects analysed	85			
Units: cells/mm^3				
arithmetic mean (confidence interval 95%)	70.4 (35.9 to 104.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with one or more Adverse Events (AEs) through study week 12

End point title	Number of participants with one or more Adverse Events (AEs) through study week 12

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product or protocol - specified procedure, whether or not considered related to the medicinal product or protocol - specified procedure. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a preexisting condition that is temporally associated with the use of the Sponsor's product, is also an AE. All randomized participants who received at least one dose of study treatment were analyzed.

End point type	Secondary

End point timeframe:

Up to Week 12

End point values	Immediate Switch to MK-1439A	Deferred Switch to MK-1439A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	43		
Units: Participants	34	34		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with one or more drug-related AEs through study week 12

End point title	Number of participants with one or more drug-related AEs through study week 12

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product or protocol - specified procedure, whether or not considered related to the medicinal product or protocol - specified procedure. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a preexisting condition that is temporally associated with the use of the Sponsor's product, is also an AE. A drug-related AE was determined by the investigator to be related to the drug. All randomized participants who received at least one dose of study treatment were analyzed.

End point type	Secondary

End point timeframe:

Up to Week 12

End point values	Immediate Switch to MK-1439A	Deferred Switch to MK-1439A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	43		
Units: Participants	14	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with one or more Serious Adverse Events (SAEs) through study week 12

End point title	Number of participants with one or more Serious Adverse Events (SAEs) through study week 12

End point description:

A serious adverse event (SAE) is any AE occurring at any dose or during any use of Sponsor's product that results in any of the following: death; is life threatening; results in persistent or significant disability/incapacity; results in or prolongs an existing hospitalization; is a congenital anomaly/birth defect; is another important medical event; is a cancer; is associated with an overdose. All randomized participants who received at least one dose of study treatment were analyzed.

End point type	Secondary

End point timeframe:

Up to Week 12

End point values	Immediate Switch to MK-1439A	Deferred Switch to MK-1439A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	43		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with one or more drug-related SAEs through study week 12

End point title	Number of participants with one or more drug-related SAEs through study week 12

End point description:

A serious adverse event (SAE) is any AE occurring at any dose or during any use of Sponsor's product that results in any of the following: death; is life threatening; results in persistent or significant disability/incapacity; results in or prolongs an existing hospitalization; is a congenital anomaly/birth defect; is another important medical event; is a cancer; is associated with an overdose. A drug-related SAE was determined by the investigator to be related to the drug. All randomized participants who received at least one dose of study treatment were analyzed.

End point type	Secondary

End point timeframe:

Up to Week 12

End point values	Immediate Switch to MK-1439A	Deferred Switch to MK-1439A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	43		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with one or more drug-related AEs for the combined treatment groups 24 weeks after the switch

End point title	Number of participants with one or more drug-related AEs for the combined treatment groups 24 weeks after the switch

End point description:

An AE was any untoward medical occurrence in a participant administered a pharmaceutical product & which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable & unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Any worsening of a preexisting condition that is temporally associated with the use of the Sponsor’s product, is also an AE. A drug-related AE was determined by the investigator to be related to the drug. For the ISG 24 week post-switch was week 24; for the DSG week 24 post-switch was week 36. All randomized participants who received ≥1 dose of study treatment, & have baseline data for analyses requiring baseline data. Per protocol, the combined treatment groups was analyzed. One participant in the DSG who discontinued from the study, before switching to MK-1439A, was not included in the analysis.

End point type	Secondary

End point timeframe:

24 weeks post-switch

End point values	Combined Treatment Groups			
Subject group type	Subject analysis set			
Number of subjects analysed	85			
Units: Participants	18			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with one or more AEs for the combined

treatment groups 24 weeks after the switch

End point title	Number of participants with one or more AEs for the combined treatment groups 24 weeks after the switch

End point description:

An AE was any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product or protocol - specified procedure, whether or not considered related to the medicinal product or protocol - specified procedure. Any worsening of a preexisting condition that is temporally associated with the use of the Sponsor's product, is also an AE. For the ISG 24 week post-switch was week 24; for the DSG week 24 post-switch was week 36. All randomized participants who received ≥1 dose of study treatment, and have baseline data for analyses requiring baseline data were analyzed. Per protocol, the combined treatment group was analyzed. One participant in the DSG who discontinued from the study, before switching to MK-1439A, was not included in the analysis.

End point type	Secondary

End point timeframe:

24 weeks post-switch

End point values	Combined Treatment Groups			
Subject group type	Subject analysis set			
Number of subjects analysed	85			
Units: Participants	71			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who discontinued treatment due to an AE through study week 12

End point title	Number of participants who discontinued treatment due to an AE through study week 12

End point description:

An AE is any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product or protocol - specified procedure, whether or not considered related to the medicinal product or protocol - specified procedure. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a preexisting condition that is temporally associated with the use of the Sponsor's product, is also an AE. All randomized participants who received at least one dose of study treatment were analyzed.

End point type	Secondary

End point timeframe:

Up to Week 12

End point values	Immediate Switch to MK-1439A	Deferred Switch to MK-1439A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	43		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with one or more SAEs for the combined treatment groups 24 weeks after the switch

End point title	Number of participants with one or more SAEs for the combined treatment groups 24 weeks after the switch

End point description:

A serious adverse event (SAE) is any AE occurring at any dose or during any use of Sponsor's product that results in any of the following: death; is life threatening; results in persistent or significant disability/incapacity; results in or prolongs an existing hospitalization; is a congenital anomaly/birth defect; is another important medical event; is a cancer; is associated with an overdose. For the ISG 24 week post-switch was week 24; for the DSG week 24 post-switch was week 36. All randomized participants who received at least one dose of study treatment, and have baseline data for analyses requiring baseline data. Based on the protocol-specified plan, the combined treatment groups was analyzed. One participant in the DSG who discontinued from the study, before switching to MK-1439A, was not included in the analysis.

End point type	Secondary

End point timeframe:

24 weeks post-switch

End point values	Combined Treatment Groups			
Subject group type	Subject analysis set			
Number of subjects analysed	85			
Units: Participants	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with one or more drug-related SAEs for the combined treatment groups 24 weeks after the switch

End point title	Number of participants with one or more drug-related SAEs for the combined treatment groups 24 weeks after the switch

End point description:

A serious adverse event (SAE) is any AE occurring at any dose or during any use of Sponsor's product that results in any of the following: death; is life threatening; results in persistent or significant disability/incapacity; results in or prolongs an existing hospitalization; is a congenital anomaly/birth defect; is another important medical event; is a cancer; is associated with an overdose. A drug-related

SAE was determined by the investigator to be related to the drug. For the ISG 24 week post-switch was week 24; for the DSG week 24 post-switch was week 36. All randomized participants who received at least one dose of study treatment, and have baseline data for analyses requiring baseline data. Based on the protocol-specified plan, the combined treatment groups was analyzed. One participant in the DSG who discontinued from the study, before switching to MK-1439A, was not included in the analysis.

End point type	Secondary

End point timeframe:

24 weeks post-switch

End point values	Combined Treatment Groups			
Subject group type	Subject analysis set			
Number of subjects analysed	85			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who discontinued treatment due to an AE for the combined treatment groups 24 weeks after the switch

End point title	Number of participants who discontinued treatment due to an AE for the combined treatment groups 24 weeks after the switch

End point description:

An AE was any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Any worsening of a preexisting condition that is temporally associated with the use of the Sponsor’s product, is also an AE. For the ISG 24 week post-switch was week 24; for the DSG week 24 post-switch was week 36. All randomized participants who received ≥1 dose of study treatment, and have baseline data for analyses requiring baseline data. Based on the protocol-specified plan, the combined treatment groups was analyzed. One participant in the DSG who discontinued from the study, before switching to MK-1439A, was not included in the analysis.

End point type	Secondary

End point timeframe:

24 weeks post-switch

End point values	Combined Treatment Groups			
Subject group type	Subject analysis set			
Number of subjects analysed	85			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 326 weeks

Adverse event reporting additional description:

All cause-mortality was reported on all allocated participants. AEs were reported for all allocated participants who received ≥1 dose of study treatment. Per protocol, serious adverse events and all-cause mortality were collected up to 326 weeks, and non-serious adverse event data were collected up to 134 weeks.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Immediate Switch Group Day 1 to Week 24

Reporting group description:

Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening switched to blinded doravirine, tenofovir, lamivudine orally, once daily for 12 weeks, followed by open-label doravirine, tenofovir, lamivudine orally, once daily for an additional 12 weeks

Reporting group title	Deferred Switch Group Double-blind Day 1 to Week 12

Reporting group description:

Participants continued their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks.

Reporting group title	Deferred Switch Group Open-label Week 12-36

Reporting group description:

Participants who continued their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks switched to open-label doravirine, tenofovir, lamivudine orally, once daily for a total of 24 weeks (Week 12 - Week 36).

Reporting group title	Immediate Switch Group only (Week 24-120) EXT 1

Reporting group description:

One doravirine, tenofovir, lamivudine taken q.d. by mouth for an additional 96 weeks (Week 24 - Week 120)

Reporting group title	Deferred Switch Group (Week 36-132) EXT 1

Reporting group description:

One doravirine, tenofovir, lamivudine taken q.d. by mouth for an additional 96 weeks (Week 36 - Week 132)

Reporting group title	Deferred Switch Group (Week 132-228) EXT 2

Reporting group description:

One doravirine, tenofovir, lamivudine taken q.d. by mouth for an additional 96 weeks (Week 132 - Week 228)

Reporting group title	Immediate Switch Group (Week 120-216) EXT 2

Reporting group description:

One doravirine, tenofovir, lamivudine taken q.d. by mouth for an additional 96 weeks (Week 120 - Week 216)

Reporting group title	Immediate Switch Group (Week 216-312) EXT 3

Reporting group description:

One doravirine, tenofovir, lamivudine taken q.d. by mouth for an additional 96 weeks (Week 216 - Week 312)

Reporting group title	Deferred Switch Group (Week 228-324) EXT 3

Reporting group description:

One doravirine, tenofovir, lamivudine taken q.d. by mouth for an additional 96 weeks (Week 228 - Week 324)

Serious adverse events	Immediate Switch Group Day 1 to Week 24	Deferred Switch Group Double-blind Day 1 to Week 12	Deferred Switch Group Open-label Week 12-36
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 43 (0.00%)	0 / 43 (0.00%)	1 / 42 (2.38%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 43 (0.00%)	0 / 43 (0.00%)	0 / 42 (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
Prostate cancer			
subjects affected / exposed	0 / 43 (0.00%)	0 / 43 (0.00%)	0 / 42 (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
Uterine leiomyoma			
subjects affected / exposed	0 / 43 (0.00%)	0 / 43 (0.00%)	0 / 42 (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			
Spinal compression fracture			
subjects affected / exposed	0 / 43 (0.00%)	0 / 43 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	0 / 43 (0.00%)	0 / 43 (0.00%)	0 / 42 (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
Stab wound			
subjects affected / exposed	0 / 43 (0.00%)	0 / 43 (0.00%)	0 / 42 (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

Nervous system disorders			
Headache			
subjects affected / exposed	0 / 43 (0.00%)	0 / 43 (0.00%)	0 / 42 (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
Pregnancy, puerperium and perinatal conditions			
Ectopic pregnancy			
subjects affected / exposed	0 / 43 (0.00%)	0 / 43 (0.00%)	0 / 42 (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			
Abdominal hernia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 43 (0.00%)	0 / 42 (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			
Cystocele			
subjects affected / exposed	0 / 43 (0.00%)	0 / 43 (0.00%)	0 / 42 (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
Psychiatric disorders			
Conversion disorder			
subjects affected / exposed	0 / 43 (0.00%)	0 / 43 (0.00%)	0 / 42 (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
Suicide attempt			
subjects affected / exposed	0 / 43 (0.00%)	0 / 43 (0.00%)	0 / 42 (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 / 43 (0.00%)	0 / 43 (0.00%)	0 / 42 (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
Pneumonia haemophilus			

subjects affected / exposed	0 / 43 (0.00%)	0 / 43 (0.00%)	0 / 42 (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
Viral infection			
subjects affected / exposed	0 / 43 (0.00%)	0 / 43 (0.00%)	0 / 42 (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
Wound sepsis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 43 (0.00%)	0 / 42 (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

Serious adverse events	Immediate Switch Group only (Week 24-120) EXT 1	Deferred Switch Group (Week 36-132) EXT 1	Deferred Switch Group (Week 132-228) EXT 2
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 43 (13.95%)	2 / 41 (4.88%)	1 / 33 (3.03%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 33 (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
Prostate cancer			
subjects affected / exposed	1 / 43 (2.33%)	0 / 41 (0.00%)	0 / 33 (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
Uterine leiomyoma			
subjects affected / exposed	1 / 43 (2.33%)	0 / 41 (0.00%)	0 / 33 (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
Injury, poisoning and procedural complications			
Spinal compression fracture			

subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 33 (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
Head injury			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 33 (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
Stab wound			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 33 (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
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 43 (2.33%)	0 / 41 (0.00%)	0 / 33 (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
Pregnancy, puerperium and perinatal conditions			
Ectopic pregnancy			
subjects affected / exposed	1 / 43 (2.33%)	0 / 41 (0.00%)	0 / 33 (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
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	1 / 43 (2.33%)	0 / 41 (0.00%)	0 / 33 (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
Reproductive system and breast disorders			
Cystocele			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	0 / 33 (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
Psychiatric disorders			
Conversion disorder			

subjects affected / exposed	1 / 43 (2.33%)	0 / 41 (0.00%)	0 / 33 (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
Suicide attempt			
subjects affected / exposed	0 / 43 (0.00%)	1 / 41 (2.44%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia haemophilus			
subjects affected / exposed	0 / 43 (0.00%)	1 / 41 (2.44%)	0 / 33 (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
Viral infection			
subjects affected / exposed	1 / 43 (2.33%)	0 / 41 (0.00%)	0 / 33 (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
Wound sepsis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 41 (0.00%)	1 / 33 (3.03%)
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	Immediate Switch Group (Week 120-216) EXT 2	Immediate Switch Group (Week 216-312) EXT 3	Deferred Switch Group (Week 228-324) EXT 3
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 39 (7.69%)	2 / 17 (11.76%)	0 / 19 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			

subjects affected / exposed	0 / 39 (0.00%)	1 / 17 (5.88%)	0 / 19 (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
Prostate cancer			
subjects affected / exposed	1 / 39 (2.56%)	0 / 17 (0.00%)	0 / 19 (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
Uterine leiomyoma			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (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			
Spinal compression fracture			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (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
Head injury			
subjects affected / exposed	0 / 39 (0.00%)	1 / 17 (5.88%)	0 / 19 (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
Stab wound			
subjects affected / exposed	1 / 39 (2.56%)	0 / 17 (0.00%)	0 / 19 (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
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (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
Pregnancy, puerperium and perinatal conditions			
Ectopic pregnancy			

subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (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			
Abdominal hernia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (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			
Cystocele			
subjects affected / exposed	1 / 39 (2.56%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Conversion disorder			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (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
Suicide attempt			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (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 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (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
Pneumonia haemophilus			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (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
Viral infection			

subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (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
Wound sepsis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (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	Immediate Switch Group Day 1 to Week 24	Deferred Switch Group Double-blind Day 1 to Week 12	Deferred Switch Group Open-label Week 12-36
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 43 (67.44%)	25 / 43 (58.14%)	26 / 42 (61.90%)
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	3 / 43 (6.98%)	4 / 43 (9.30%)	4 / 42 (9.52%)
occurrences (all)	4	4	4
Somnolence			
subjects affected / exposed	6 / 43 (13.95%)	3 / 43 (6.98%)	5 / 42 (11.90%)
occurrences (all)	8	3	5
Headache			
subjects affected / exposed	11 / 43 (25.58%)	7 / 43 (16.28%)	3 / 42 (7.14%)
occurrences (all)	13	9	3
Dizziness			
subjects affected / exposed	7 / 43 (16.28%)	5 / 43 (11.63%)	5 / 42 (11.90%)
occurrences (all)	7	5	5
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 43 (0.00%)	1 / 43 (2.33%)	0 / 42 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	6 / 43 (13.95%)	3 / 43 (6.98%)	4 / 42 (9.52%)
occurrences (all)	6	3	4
Nausea			

subjects affected / exposed	5 / 43 (11.63%)	1 / 43 (2.33%)	1 / 42 (2.38%)
occurrences (all)	5	1	1
Respiratory, thoracic and mediastinal disorders			
Productive cough			
subjects affected / exposed	0 / 43 (0.00%)	2 / 43 (4.65%)	0 / 42 (0.00%)
occurrences (all)	0	2	0
Cough			
subjects affected / exposed	2 / 43 (4.65%)	0 / 43 (0.00%)	2 / 42 (4.76%)
occurrences (all)	2	0	2
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	3 / 43 (6.98%)	1 / 43 (2.33%)	1 / 42 (2.38%)
occurrences (all)	4	1	1
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	5 / 43 (11.63%)	3 / 43 (6.98%)	3 / 42 (7.14%)
occurrences (all)	5	3	3
Aggression			
subjects affected / exposed	3 / 43 (6.98%)	2 / 43 (4.65%)	2 / 42 (4.76%)
occurrences (all)	4	2	2
Anxiety			
subjects affected / exposed	2 / 43 (4.65%)	2 / 43 (4.65%)	7 / 42 (16.67%)
occurrences (all)	3	2	7
Confusional state			
subjects affected / exposed	1 / 43 (2.33%)	1 / 43 (2.33%)	3 / 42 (7.14%)
occurrences (all)	1	1	3
Depressed mood			
subjects affected / exposed	1 / 43 (2.33%)	2 / 43 (4.65%)	0 / 42 (0.00%)
occurrences (all)	1	2	0
Insomnia			
subjects affected / exposed	8 / 43 (18.60%)	7 / 43 (16.28%)	6 / 42 (14.29%)
occurrences (all)	9	10	6
Depression			
subjects affected / exposed	3 / 43 (6.98%)	1 / 43 (2.33%)	4 / 42 (9.52%)
occurrences (all)	3	1	4
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	3 / 43 (6.98%)	1 / 43 (2.33%)	1 / 42 (2.38%)
occurrences (all)	4	1	1
Arthralgia			
subjects affected / exposed	7 / 43 (16.28%)	1 / 43 (2.33%)	2 / 42 (4.76%)
occurrences (all)	8	1	2
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 43 (4.65%)	2 / 43 (4.65%)	2 / 42 (4.76%)
occurrences (all)	2	2	2
Upper respiratory tract infection			
subjects affected / exposed	4 / 43 (9.30%)	6 / 43 (13.95%)	2 / 42 (4.76%)
occurrences (all)	6	6	2
Viral infection			
subjects affected / exposed	1 / 43 (2.33%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences (all)	1	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 43 (0.00%)	1 / 43 (2.33%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 43 (0.00%)	0 / 43 (0.00%)	1 / 42 (2.38%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	3 / 43 (6.98%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences (all)	3	0	0
Influenza			
subjects affected / exposed	2 / 43 (4.65%)	0 / 43 (0.00%)	2 / 42 (4.76%)
occurrences (all)	2	0	2

Non-serious adverse events	Immediate Switch Group only (Week 24-120) EXT 1	Deferred Switch Group (Week 36-132) EXT 1	Deferred Switch Group (Week 132-228) EXT 2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 43 (72.09%)	33 / 41 (80.49%)	0 / 33 (0.00%)
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	4 / 43 (9.30%)	5 / 41 (12.20%)	0 / 33 (0.00%)
occurrences (all)	5	5	0

Somnolence			
subjects affected / exposed	9 / 43 (20.93%)	7 / 41 (17.07%)	0 / 33 (0.00%)
occurrences (all)	9	9	0
Headache			
subjects affected / exposed	8 / 43 (18.60%)	14 / 41 (34.15%)	0 / 33 (0.00%)
occurrences (all)	8	15	0
Dizziness			
subjects affected / exposed	5 / 43 (11.63%)	5 / 41 (12.20%)	0 / 33 (0.00%)
occurrences (all)	5	5	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 43 (4.65%)	4 / 41 (9.76%)	0 / 33 (0.00%)
occurrences (all)	2	4	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 43 (2.33%)	4 / 41 (9.76%)	0 / 33 (0.00%)
occurrences (all)	1	4	0
Nausea			
subjects affected / exposed	1 / 43 (2.33%)	2 / 41 (4.88%)	0 / 33 (0.00%)
occurrences (all)	1	2	0
Respiratory, thoracic and mediastinal disorders			
Productive cough			
subjects affected / exposed	3 / 43 (6.98%)	1 / 41 (2.44%)	0 / 33 (0.00%)
occurrences (all)	3	1	0
Cough			
subjects affected / exposed	3 / 43 (6.98%)	2 / 41 (4.88%)	0 / 33 (0.00%)
occurrences (all)	3	2	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 43 (0.00%)	1 / 41 (2.44%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	5 / 43 (11.63%)	5 / 41 (12.20%)	0 / 33 (0.00%)
occurrences (all)	6	5	0
Aggression			

subjects affected / exposed	4 / 43 (9.30%)	7 / 41 (17.07%)	0 / 33 (0.00%)
occurrences (all)	4	7	0
Anxiety			
subjects affected / exposed	7 / 43 (16.28%)	11 / 41 (26.83%)	0 / 33 (0.00%)
occurrences (all)	7	11	0
Confusional state			
subjects affected / exposed	6 / 43 (13.95%)	6 / 41 (14.63%)	0 / 33 (0.00%)
occurrences (all)	6	7	0
Depressed mood			
subjects affected / exposed	5 / 43 (11.63%)	2 / 41 (4.88%)	0 / 33 (0.00%)
occurrences (all)	6	2	0
Insomnia			
subjects affected / exposed	5 / 43 (11.63%)	10 / 41 (24.39%)	0 / 33 (0.00%)
occurrences (all)	5	13	0
Depression			
subjects affected / exposed	5 / 43 (11.63%)	8 / 41 (19.51%)	0 / 33 (0.00%)
occurrences (all)	7	8	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	5 / 43 (11.63%)	2 / 41 (4.88%)	0 / 33 (0.00%)
occurrences (all)	6	2	0
Arthralgia			
subjects affected / exposed	4 / 43 (9.30%)	3 / 41 (7.32%)	0 / 33 (0.00%)
occurrences (all)	4	3	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 43 (9.30%)	2 / 41 (4.88%)	0 / 33 (0.00%)
occurrences (all)	5	5	0
Upper respiratory tract infection			
subjects affected / exposed	4 / 43 (9.30%)	7 / 41 (17.07%)	0 / 33 (0.00%)
occurrences (all)	5	8	0
Viral infection			
subjects affected / exposed	1 / 43 (2.33%)	3 / 41 (7.32%)	0 / 33 (0.00%)
occurrences (all)	1	3	0
Lower respiratory tract infection			

subjects affected / exposed	4 / 43 (9.30%)	4 / 41 (9.76%)	0 / 33 (0.00%)
occurrences (all)	4	4	0
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 43 (4.65%)	3 / 41 (7.32%)	0 / 33 (0.00%)
occurrences (all)	3	5	0
Gastroenteritis			
subjects affected / exposed	0 / 43 (0.00%)	2 / 41 (4.88%)	0 / 33 (0.00%)
occurrences (all)	0	2	0
Influenza			
subjects affected / exposed	4 / 43 (9.30%)	0 / 41 (0.00%)	0 / 33 (0.00%)
occurrences (all)	5	0	0

Non-serious adverse events	Immediate Switch Group (Week 120-216) EXT 2	Immediate Switch Group (Week 216-312) EXT 3	Deferred Switch Group (Week 228-324) EXT 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0

Nausea			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Productive cough			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Aggression			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Depressed mood			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 39 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 October 2016	The primary purpose of Amendment 1 was to add study extension 1 to collect long-term efficacy and safety data and to incorporate changes to facilitate enrollment and ensure trial completion.
13 July 2018	The primary purpose of Amendment 2 was to add study extension 2 to provide continued access to MK-1439A for participants who are deriving benefit from MK-1439A until the drug is available locally in the country participating in the trial or for an additional 2 years.
18 March 2021	The primary purpose of Amendment 3 was to provide continued access to MK-1439A until the drug is available locally in countries participating in the trial or for an additional 2 years (whichever comes first).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported