



Clinical trial results:

A Phase IIa Multicenter, Open-Label Clinical Trial to Evaluate the Safety and Efficacy of MK-1439A in Treatment-Naïve HIV-1 Infected Subjects With Selected Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI) Transmitted Resistance Mutations

Summary

EudraCT number	2015-003616-20
Trial protocol	GB FR
Global end of trial date	28 October 2020

Results information

Result version number	v1 (current)
This version publication date	01 October 2021
First version publication date	01 October 2021

Trial information

Trial identification

Sponsor protocol code	1439A-030
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02629822
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.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	28 October 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 November 2018
Global end of trial reached?	Yes
Global end of trial date	28 October 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study are to evaluate the antiretroviral activity and the safety/tolerability of open-label doravirine/lamivudine/tenofovir disoproxil fumarate (DOR/3TC/TDF; MK-1439A; DELSTRIGO™) consisting of a single fixed-dose combination (FDC) tablet of DOR/3TC/TDF 100 mg/300 mg/300 mg in treatment-naïve HIV-1 infected participants with select non-nucleoside reverse transcriptase inhibitor (NNRTI) transmitted resistance-associated mutations. This study had a Base Study (Day 1 to Week 96) and an optional Study Extension (Week 96 to Week 192).

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	14 January 2016
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	24 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	United States: 3
Worldwide total number of subjects	10
EEA total number of subjects	3

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)	10
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were enrolled at study sites in Canada, France, Spain, UK, and USA.

Period 1

Period 1 title	Base Study
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	DOR/3TC/TDF
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Arm description:

Treatment-naïve HIV-1 infected participants with NNRTI transmitted resistance-associated mutations were treated with open-label MK-1439A (DOR/3TC/TDF 100mg/300mg/300mg) as a FDC tablet taken once daily by mouth for 96 weeks in the Base Study. In addition, eligible participants continued to receive the same MK-1439A regimen from Week 96 to Week 192 during the optional Extension Study.

Arm type	Experimental
Investigational medicinal product name	Doravirine/lamivudine/tenofovir disoproxil fumarate
Investigational medicinal product code	
Other name	MK-1439A DELSTRIGO™
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

MK-1439A FDC tablet of MK-1439 (doravirine) 100 mg / lamivudine 300 mg / tenofovir disoproxil fumarate 300 mg taken by mouth.

Number of subjects in period 1	DOR/3TC/TDF
Started	10
Completed	7
Not completed	3
Non-Compliance With Study Drug	1
Lost to follow-up	2

Period 2

Period 2 title	Extension Study
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	DOR/3TC/TDF
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Arm description:

Treatment-naïve HIV-1 infected participants with NNRTI transmitted resistance-associated mutations were treated with open-label MK-1439A (DOR/3TC/TDF 100mg/300mg/300mg) as a FDC tablet taken once daily by mouth for 96 weeks in the Base Study. In addition, eligible participants continued to receive the same MK-1439A regimen from Week 96 to Week 192 during the Extension Study.

Arm type	Experimental
Investigational medicinal product name	Doravirine/lamivudine/tenofovir disoproxil fumarate
Investigational medicinal product code	
Other name	MK-1439A DELSTRIGO™
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

MK-1439A FDC tablet of MK-1439 (doravirine) 100 mg / lamivudine 300 mg / tenofovir disoproxil fumarate 300 mg taken by mouth.

Number of subjects in period 2 ^[1]	DOR/3TC/TDF
Started	6
Completed	4
Not completed	2
Adverse event, non-fatal	1
Lost to follow-up	1

Notes:

[1] - 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: Participation in the Extension Study was optional.

Baseline characteristics

Reporting groups

Reporting group title	DOR/3TC/TDF
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Reporting group description:

Treatment-naïve HIV-1 infected participants with NNRTI transmitted resistance-associated mutations were treated with open-label MK-1439A (DOR/3TC/TDF 100mg/300mg/300mg) as a FDC tablet taken once daily by mouth for 96 weeks in the Base Study. In addition, eligible participants continued to receive the same MK-1439A regimen from Week 96 to Week 192 during the optional Extension Study.

Reporting group values	DOR/3TC/TDF	Total	
Number of subjects	10	10	
Age categorical			
Units: Participants			
Adults (18-64 years)	10	10	
Age Continuous			
Units: Years			
arithmetic mean	37.1		
standard deviation	± 32.5	-	
Sex: Female, Male			
Units: Participants			
Female	2	2	
Male	8	8	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	1	1	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	3	3	
White	5	5	
More than one race	0	0	
Unknown or Not Reported	1	1	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	2	2	
Not Hispanic or Latino	6	6	
Unknown or Not Reported	2	2	

End points

End points reporting groups

Reporting group title	DOR/3TC/TDF
Reporting group description: Treatment-naïve HIV-1 infected participants with NNRTI transmitted resistance-associated mutations were treated with open-label MK-1439A (DOR/3TC/TDF 100mg/300mg/300mg) as a FDC tablet taken once daily by mouth for 96 weeks in the Base Study. In addition, eligible participants continued to receive the same MK-1439A regimen from Week 96 to Week 192 during the optional Extension Study.	
Reporting group title	DOR/3TC/TDF
Reporting group description: Treatment-naïve HIV-1 infected participants with NNRTI transmitted resistance-associated mutations were treated with open-label MK-1439A (DOR/3TC/TDF 100mg/300mg/300mg) as a FDC tablet taken once daily by mouth for 96 weeks in the Base Study. In addition, eligible participants continued to receive the same MK-1439A regimen from Week 96 to Week 192 during the Extension Study.	

Primary: Percentage of Participants Achieving HIV-1 Ribonucleic Acid (RNA) <50 Copies/mL of Plasma at Week 48

End point title	Percentage of Participants Achieving HIV-1 Ribonucleic Acid (RNA) <50 Copies/mL of Plasma at Week 48 ^[1]
End point description: The percentage of participants achieving HIV-1 ribonucleic acid (RNA) <50 copies/mL in plasma at Week 48 was calculated. The Abbott RealTime HIV-1 Assay, which has a lower limit of reliable quantification (LoQ) of 40 copies/mL, was used to measure the HIV-1 RNA level in plasma samples obtained at Week 48 visit. All participants who received ≥1 dose of MK-1439A, had baseline and Week 48 data for HIV in plasma, and whose central lab results confirmed the presence of protocol-specified NNRTI resistance-associated mutations were included.	
End point type	Primary
End point timeframe: Week 48	
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: Per protocol, only descriptive statistics are presented.	

End point values	DOR/3TC/TDF			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Percentage of Participants				
number (confidence interval 95%)	100.0 (63.1 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Experiencing ≥1 Adverse Events (AE) up to Week 48

End point title	Percentage of Participants Experiencing ≥1 Adverse Events (AE) up to Week 48 ^[2]
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End point description:

The percentage of participants experiencing ≥ 1 AE up to Week 48 was calculated. An AE was defined as any unfavorable and unintended sign, symptom, or disease (new or worsening) temporally associated with the use of study therapy, regardless of whether or not a causal relationship with the study therapy could be determined. All participants who received ≥ 1 dose of MK-1439A were included.

End point type	Primary
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End point timeframe:

Up to Week 48

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Per protocol, only descriptive statistics are presented.

End point values	DOR/3TC/TDF			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Percentage of Participants				
number (not applicable)	90.0			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants who discontinued treatment due to an AE up to Week 48

End point title	Percentage of participants who discontinued treatment due to an AE up to Week 48 ^[3]
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End point description:

The percentage of participants who discontinued from study medication due to an adverse event was calculated. An AE was defined as any unfavorable and unintended sign, symptom, or disease (new or worsening) temporally associated with the use of study therapy, regardless of whether or not a causal relationship with the study therapy could be determined. All participants who received ≥ 1 dose of MK-1439A were included.

End point type	Primary
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End point timeframe:

Up to Week 48

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: Per protocol, only descriptive statistics are presented.

End point values	DOR/3TC/TDF			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Percentage of Participants				
number (not applicable)	0.0			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Experiencing ≥ 1 Adverse Events (AE) up to Week 96

End point title	Percentage of Participants Experiencing ≥ 1 Adverse Events (AE) up to Week 96 ^[4]
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End point description:

The percentage of participants experiencing ≥ 1 AE up to Week 96 was calculated. An AE was defined as any unfavorable and unintended sign, symptom, or disease (new or worsening) temporally associated with the use of study therapy, regardless of whether or not a causal relationship with the study therapy could be determined. All participants who received ≥ 1 dose of MK-1439A were included.

End point type	Primary
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End point timeframe:

Up to Week 96

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: Per protocol, only descriptive statistics are presented.

End point values	DOR/3TC/TDF			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Percentage of Participants				
number (not applicable)	90.0			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Discontinued Treatment Due to an AE up to Week 96

End point title	Percentage of Participants Who Discontinued Treatment Due to an AE up to Week 96 ^[5]
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End point description:

The percentage of participants who discontinued from study medication due to an adverse event was calculated. An AE was defined as any unfavorable and unintended sign, symptom, or disease (new or worsening) temporally associated with the use of study therapy, regardless of whether or not a causal relationship with the study therapy could be determined. All participants who received ≥ 1 dose of MK-1439A were included.

End point type	Primary
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End point timeframe:

Up to Week 96

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Per protocol, only descriptive statistics are presented.

End point values	DOR/3TC/TDF			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Percentage of Participants				
number (not applicable)	0.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving HIV-1 Ribonucleic Acid (RNA) <50 Copies/mL of Plasma at Week 96

End point title	Percentage of Participants Achieving HIV-1 Ribonucleic Acid (RNA) <50 Copies/mL of Plasma at Week 96
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End point description:

The percentage of participants achieving HIV-1 ribonucleic acid (RNA) <50 copies/mL in plasma at Week 96 was calculated. The Abbott RealTime HIV-1 Assay, which has a lower limit of reliable quantification (LoQ) of 40 copies/mL, was used to measure the HIV-1 RNA level in plasma samples obtained at Week 96 visit. All participants who received ≥1 dose of MK-1439A, had baseline and Week 96 data for HIV in plasma, and whose central lab results confirmed the presence of protocol-specified NNRTI resistance-associated mutations were included.

End point type	Secondary
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End point timeframe:

Week 96

End point values	DOR/3TC/TDF			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Percentage of Participants				
number (confidence interval 95%)	100.0 (59.0 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving HIV-1 Ribonucleic Acid (RNA) <40 Copies/mL of Plasma at Week 48

End point title	Percentage of Participants Achieving HIV-1 Ribonucleic Acid (RNA) <40 Copies/mL of Plasma at Week 48
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End point description:

The percentage of participants achieving HIV-1 ribonucleic acid (RNA) <40 copies/mL in plasma at Week 48 was calculated. The Abbott RealTime HIV-1 Assay, which has a lower limit of reliable quantification (LoQ) of 40 copies/mL, was used to measure the HIV-1 RNA level in plasma samples obtained at Week 48 visit. Participants with reading below the LoQ were considered to have <40 copies/mL. All participants who received ≥1 dose of MK-1439A, had baseline and Week 48 data for HIV in plasma, and whose central lab results confirmed the presence of protocol-specified NNRTI resistance-associated

mutations were included.

End point type	Secondary
End point timeframe:	
Week 48	

End point values	DOR/3TC/TDF			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Percentage of Participants				
number (confidence interval 95%)	100.0 (63.1 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving HIV-1 Ribonucleic Acid (RNA) <40 Copies/mL of Plasma at Week 96

End point title	Percentage of Participants Achieving HIV-1 Ribonucleic Acid (RNA) <40 Copies/mL of Plasma at Week 96
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End point description:

The percentage of participants achieving HIV-1 ribonucleic acid (RNA) <40 copies/mL in plasma at Week 96 was calculated. The Abbott RealTime HIV-1 Assay, which has a lower limit of reliable quantification (LoQ) of 40 copies/mL, was used to measure the HIV-1 RNA level in plasma samples obtained at Week 96 visit. Participants with reading below the LoQ were considered to have <40 copies/mL. All participants who received ≥1 dose of MK-1439A, had baseline and Week 96 data for HIV in plasma, and whose central lab results confirmed the presence of protocol-specified NNRTI resistance-associated mutations were included.

End point type	Secondary
End point timeframe:	
Week 96	

End point values	DOR/3TC/TDF			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Percentage of Participants				
number (confidence interval 95%)	100.0 (59.0 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CD4 Cell Count at Week 48

End point title	Change from Baseline in CD4 Cell Count at Week 48
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End point description:

The change from baseline in CD4 cell count at Week 48 was calculated. All participants who received ≥ 1 dose of MK-1439A, had baseline and Week 48 data for CD4 cell count, and whose central lab results confirmed the presence of protocol-specified NNRTI resistance-associated mutations were included.

End point type	Secondary
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End point timeframe:

Baseline (Day 1) and Week 48

End point values	DOR/3TC/TDF			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Cells/mm ³				
arithmetic mean (confidence interval 95%)				
Baseline for the Week 48 Population	409 (293.5 to 525.0)			
Change from Baseline at Week 48	132 (24.4 to 239.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CD4 Cell Count at Week 96

End point title	Change from Baseline in CD4 Cell Count at Week 96
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End point description:

The change from baseline in CD4 cell count at Week 96 was calculated. All participants who received ≥ 1 dose of MK-1439A, had baseline and Week 96 data for CD4 cell count, and whose central lab results confirmed the presence of protocol-specified NNRTI resistance-associated mutations were included.

End point type	Secondary
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End point timeframe:

Baseline (Day 1) and Week 96

End point values	DOR/3TC/TDF			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Cells/mm ³				
arithmetic mean (confidence interval 95%)				
Baseline for the Week 96 Population	437 (323.9 to 550.7)			
Change from Baseline at Week 96	153 (23.0 to 282.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Loss of Virologic Response

End point title	Time to Loss of Virologic Response
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End point description:

The time to loss of virologic response (TLOVR) was reported. For participants who achieved HIV-1 RNA <50 copies/mL of plasma and subsequently had two consecutive HIV-1 RNA values of ≥50 copies/mL measured at least 1 week apart, TLOVR was the time between Day 1 and the date of the first of the two consecutive values ≥50 copies/mL. For participants who achieved and sustained HIV-1 RNA <50 copies/mL, time to loss of virologic response was censored at the time of the last available measurement. All participants who experienced protocol-defined virologic failure, received ≥1 dose of MK-1439A, had baseline and later data for HIV in plasma, and whose central lab results confirmed the presence of protocol-specified NNRTI resistance-associated mutations were included. Participants who did not experience virologic failure were excluded from the analysis population.

End point type	Secondary
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End point timeframe:

Up to Week 96

End point values	DOR/3TC/TDF			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Days				
arithmetic mean (full range (min-max))	166 (166 to 166)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants Achieving HIV-1 Ribonucleic Acid (RNA) <50 Copies/mL of Plasma at Week 192

End point title	Percentage of Participants Achieving HIV-1 Ribonucleic Acid (RNA) <50 Copies/mL of Plasma at Week 192
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End point description:

The percentage of participants achieving HIV-1 ribonucleic acid (RNA) <50 copies/mL in plasma at Week 192 was calculated. The Abbott RealTime HIV-1 Assay, which has a lower limit of reliable quantification (LoQ) of 40 copies/mL, was used to measure the HIV-1 RNA level in plasma samples obtained at Week 192 visit. All participants who received ≥1 dose of MK-1439A, had baseline and Week 192 data for HIV in plasma, and whose central lab results confirmed the presence of protocol-specified NNRTI resistance-associated mutations were included.

End point type	Other pre-specified
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End point timeframe:

Week 192

End point values	DOR/3TC/TDF			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Percentage of Participants				
number (confidence interval 95%)	100.0 (39.8 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants Achieving HIV-1 Ribonucleic Acid (RNA) <40 Copies/mL of Plasma at Week 192

End point title	Percentage of Participants Achieving HIV-1 Ribonucleic Acid (RNA) <40 Copies/mL of Plasma at Week 192
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End point description:

The percentage of participants achieving HIV-1 ribonucleic acid (RNA) <40 copies/mL in plasma at Week 192 was calculated. The Abbott RealTime HIV-1 Assay, which has a lower limit of reliable quantification (LoQ) of 40 copies/mL, was used to measure the HIV-1 RNA level in plasma samples obtained at Week 192 visit. Participants with reading below the LoQ were considered to have <40 copies/mL. All participants who received ≥ 1 dose of MK-1439A, had baseline and Week 192 data for HIV in plasma, and whose central lab results confirmed the presence of protocol-specified NNRTI resistance-associated mutations were included.

End point type	Other pre-specified
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End point timeframe:

Week 192

End point values	DOR/3TC/TDF			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Percentage of Participants				
number (confidence interval 95%)	100.0 (39.8 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline in CD4 Cell Count at Week 192

End point title	Change from Baseline in CD4 Cell Count at Week 192
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End point description:

The change from baseline in CD4 cell count at Week 192 was calculated. All participants who received ≥ 1 dose of MK-1439A, had baseline and Week 192 data for CD4 cell count, and whose central lab results confirmed the presence of protocol-specified NNRTI resistance-associated mutations were included.

End point type

Other pre-specified

End point timeframe:

Baseline (Day 1) and Week 192

End point values	DOR/3TC/TDF			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Cells/mm ³				
arithmetic mean (confidence interval 95%)				
Baseline for the Week 192 Population	479 (310.0 to 648.5)			
Change from Baseline at Week 192	196 (27.4 to 364.1)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 192 weeks

Adverse event reporting additional description:

All participants who received ≥ 1 dose of study intervention are included in AE results. All-cause mortality is based on all randomized participants.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.1
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Reporting groups

Reporting group title	DOR/3TC/TDF Study Extension: Week 97 to Week 192
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Reporting group description:

Treatment-naïve HIV-1 infected participants with NNRTI transmitted resistance-associated mutations were treated with open-label MK-1439A (DOR/3TC/TDF 100mg/300mg/300mg) as a FDC tablet taken once daily by mouth from Day 1 to Week 96 in the Base Study.

Reporting group title	DOR/3TC/TDF Base Study: Day 1 to Week 96
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Reporting group description:

Treatment-naïve HIV-1 infected participants with NNRTI transmitted resistance-associated mutations were treated with open-label MK-1439A (DOR/3TC/TDF 100mg/300mg/300mg) as a FDC tablet taken once daily by mouth from Week 96 to Week 192 in the optional Extension Study.

Serious adverse events	DOR/3TC/TDF Study Extension: Week 97 to Week 192	DOR/3TC/TDF Base Study: Day 1 to Week 96	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Immune system disorders			
Allergy to arthropod sting			
subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	DOR/3TC/TDF Study Extension: Week 97 to Week 192	DOR/3TC/TDF Base Study: Day 1 to Week 96	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)	9 / 10 (90.00%)	

Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Exposure to communicable disease			
subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	2	
Eye contusion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Fall			
subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Hand fracture			
subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Dysaesthesia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Dystonia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Sciatica			
subjects affected / exposed	0 / 6 (0.00%)	2 / 10 (20.00%)	
occurrences (all)	0	2	
Taste disorder			
subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	

General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	2 / 10 (20.00%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	2 / 10 (20.00%)	
occurrences (all)	0	4	
Abdominal pain			
subjects affected / exposed	1 / 6 (16.67%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Constipation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Anogenital dysplasia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	1 / 6 (16.67%)	2 / 10 (20.00%)	
occurrences (all)	1	2	
Defaecation urgency			
subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	2 / 10 (20.00%)	
occurrences (all)	0	4	
Gastrointestinal tract irritation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Dry mouth			
subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Vomiting			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 10 (10.00%) 3	
Reproductive system and breast disorders Menstruation irregular subjects affected / exposed occurrences (all) Penile discharge subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1 0 / 6 (0.00%) 0	0 / 10 (0.00%) 0 1 / 10 (10.00%) 1	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all) Sinus congestion subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0	1 / 10 (10.00%) 2 1 / 10 (10.00%) 1 1 / 10 (10.00%) 1 1 / 10 (10.00%) 1	
Skin and subcutaneous tissue disorders Photosensitivity reaction subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0 0 / 6 (0.00%) 0	1 / 10 (10.00%) 1 1 / 10 (10.00%) 1	
Psychiatric disorders Abnormal dreams subjects affected / exposed occurrences (all) Depression subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0 1 / 6 (16.67%) 1	1 / 10 (10.00%) 1 0 / 10 (0.00%) 0	

Insomnia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 10 (10.00%) 1	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Neck pain subjects affected / exposed occurrences (all)	 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0	 2 / 10 (20.00%) 2 4 / 10 (40.00%) 4 2 / 10 (20.00%) 2	
Infections and infestations Chlamydial infection subjects affected / exposed occurrences (all) Bronchitis subjects affected / exposed occurrences (all) Hepatitis syphilitic subjects affected / exposed occurrences (all) Gonorrhoea subjects affected / exposed occurrences (all) Folliculitis subjects affected / exposed occurrences (all) Herpes simplex subjects affected / exposed occurrences (all) Infected cyst subjects affected / exposed occurrences (all) Lower respiratory tract infection	 1 / 6 (16.67%) 1 1 / 6 (16.67%) 1 0 / 6 (0.00%) 0 1 / 6 (16.67%) 1 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0	 0 / 10 (0.00%) 0 0 / 10 (0.00%) 0 1 / 10 (10.00%) 1 0 / 10 (0.00%) 0 1 / 10 (10.00%) 1 1 / 10 (10.00%) 1 1 / 10 (10.00%) 1	

subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	1 / 6 (16.67%)	3 / 10 (30.00%)	
occurrences (all)	2	5	
Influenza			
subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Otitis externa			
subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Oropharyngeal gonococcal infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Secondary syphilis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Proctitis gonococcal			
subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Shigella infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Sinusitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 6 (16.67%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Hyperlipidaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Vitamin D deficiency			
subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 August 2016	AM1: The purpose for this amendment was to update study design and provide rationale/enrollment criteria for the Extension Study.
05 June 2017	AM2: The purpose of this amendment was to change the enrollment target.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported