Clinical trial results:
Multicenter, Double-Blind, Randomized, 2-Part, Dose Ranging Study to Compare the Safety, and Antiretroviral Activity of MK-1439 Plus TRUVADA Versus Efavirenz Plus TRUVADA in Antiretroviral Treatment-Naive, HIV-1 Infected Patients

Summary

EudraCT number	2012-001573-93
Trial protocol	DE ES BE NL PL
Global end of trial date	21 March 2016

Results information

Result version number	v1 (current)
This version publication date	01 April 2017
First version publication date	01 April 2017

Trial information

Trial identification

Sponsor protocol code	1439-007

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01632345
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	31 December 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 December 2014
Global end of trial reached?	Yes
Global end of trial date	21 March 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Part 1 - Dose-Ranging. Evaluated the (1) safety and tolerability and (2) efficacy (antiretroviral activity) of 4 doses of doravirine (MK-1439) compared with efavirenz, each given in combination with TRUVADA® (emtricitabine 200 mg + tenofovir disoproxil fumarate 300 mg) for at least 24 weeks. A single dose of doravirine was selected for further study after all participants completed the Week 24 visit. Part 2 - Selected Dose. Evaluated the safety of the selected dose of doravirine compared with efavirenz through Week 96, particularly with regard to early onset (by Week 8 and 24) of central nervous system adverse events (CNS events). The hypothesis tested in this study was that MK-1439 at the final dose selected is superior to efavirenz, each given in combination with TRUVADA, as measured by the proportion of participants with CNS events by Week 8. If superiority was established at Week 8, the same hypothesis was tested for Week 24.

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	15 October 2012
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	Australia: 31
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Canada: 14
Country: Number of subjects enrolled	France: 17
Country: Number of subjects enrolled	Germany: 56
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Puerto Rico: 27
Country: Number of subjects enrolled	Romania: 26
Country: Number of subjects enrolled	Russian Federation: 16
Country: Number of subjects enrolled	Spain: 45
Country: Number of subjects enrolled	United States: 100
Worldwide total number of subjects	340
EEA total number of subjects	152

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)	336
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study enrolled 342 treatment-naïve HIV-infected participants, 18 years of age or older with baseline HIV RNA of at least 1,000 copies/mL and baseline CD4 cell counts of at least 100 cells/mm3. Two of the enrolled participants never received treatment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Doravirine 25 mg: Part I

Arm description:

Doravirine (MK-1439) 25 mg once daily plus TRUVADA once daily

Arm type	Experimental
Investigational medicinal product name	Doravirine
Investigational medicinal product code	MK-1439
Other name	
Pharmaceutical forms	Tablet, Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg administered once daily plus TRUVADA administered once daily

Arm title	Doravirine 50 mg: Part I

Arm description:

Doravirine (MK-1439) 50 mg once daily plus TRUVADA once daily

Arm type	Experimental
Investigational medicinal product name	Doravirine
Investigational medicinal product code	MK-1439
Other name	
Pharmaceutical forms	Tablet, Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

50 mg administered once daily plus TRUVADA administered once daily

Arm title	Doravirine 100 mg: Part I

Arm description:

Doravirine (MK-1439) 100 mg once daily plus TRUVADA once daily

Arm type	Experimental
Investigational medicinal product name	Doravirine
Investigational medicinal product code	MK-1439
Other name	
Pharmaceutical forms	Tablet, Film-coated tablet
Routes of administration	Oral use

Dosage and administration details: 100 mg administered once daily plus TRUVADA administered once daily	

Arm title	Doravirine 200 mg: Part I
Arm description: Doravirine (MK-1439) 200 mg once daily plus TRUVADA once daily	
Arm type	Experimental
Investigational medicinal product name	Doravirine
Investigational medicinal product code	MK-1439
Other name	
Pharmaceutical forms	Tablet, Film-coated tablet
Routes of administration	Oral use
Dosage and administration details: 200 mg administered once daily plus TRUVADA administered once daily	
Arm title	Efavirenz 600 mg: Part I
Arm description: Efavirenz 600 mg once daily plus TRUVADA once daily	
Arm type	Active comparator
Investigational medicinal product name	Efavirenz
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details: 600 mg administered once daily plus TRUVADA administered once daily	
Arm title	Doravirine 100 mg: Part II
Arm description: Doravirine (MK-1439) 100 mg once daily plus TRUVADA once daily	
Arm type	Experimental
Investigational medicinal product name	Doravirine
Investigational medicinal product code	MK-1439
Other name	
Pharmaceutical forms	Tablet, Film-coated tablet
Routes of administration	Oral use
Dosage and administration details: 100 mg administered once daily plus TRUVADA administered once daily	
Arm title	Efavirenz 600 mg: Part II
Arm description: Efavirenz 600 mg once daily plus TRUVADA once daily	
Arm type	Active comparator
Investigational medicinal product name	Efavirenz
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details: 600 mg administered once daily plus TRUVADA administered once daily	

Number of subjects in period 1	Doravirine 25 mg: Part I	Doravirine 50 mg: Part I	Doravirine 100 mg: Part I
Started	40	43	42
Completed	28	28	32
Not completed	12	15	10
Physician decision	2	1	-
Adverse event, non-fatal	1	4	2
Pregnancy	-	1	-
Non-compliance with study drug	3	2	2
Participant withdrawal	3	4	4
Lost to follow-up	3	2	1
Lack of efficacy	-	1	-
Protocol deviation	-	-	1

Number of subjects in period 1	Doravirine 200 mg: Part I	Efavirenz 600 mg: Part I	Doravirine 100 mg: Part II
Started	41	42	66
Completed	33	29	55
Not completed	8	13	11
Physician decision	-	1	-
Adverse event, non-fatal	1	3	3
Pregnancy	-	-	-
Non-compliance with study drug	1	-	3
Participant withdrawal	1	4	2
Lost to follow-up	3	4	3
Lack of efficacy	1	1	-
Protocol deviation	1	-	-

Number of subjects in period 1	Efavirenz 600 mg: Part II
Started	66
Completed	55
Not completed	11
Physician decision	-
Adverse event, non-fatal	8
Pregnancy	-
Non-compliance with study drug	-
Participant withdrawal	2
Lost to follow-up	1
Lack of efficacy	-
Protocol deviation	-

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study
Reporting group description:	
Randomised/Treated Participants	

Reporting group values	Overall Study	Total	
Number of subjects	340	340	
Age Categorical			
Two randomised participants who were enrolled in the overall population (n=342) never received treatment.			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	336	336	
From 65-84 years	4	4	
85 years and over	0	0	
Age Continuous			
Two enrolled participants in the overall population who were randomized (n=342) never received treatment.			
Units: years			
arithmetic mean	36.4		
full range (min-max)	19 to 69	-	
Gender Categorical			
Units: Subjects			
Female	315	315	
Male	25	25	

Subject analysis sets	
Subject analysis set title	Doravirine 25 mg: Part I
Subject analysis set type	Safety analysis
Subject analysis set description:	
Doravirine (MK-1439) 25 mg once daily plus TRUVADA once daily	
Subject analysis set title	Doravirine 50 mg: Part I
Subject analysis set type	Safety analysis
Subject analysis set description:	
Doravirine (MK-1439) 50 mg once daily plus TRUVADA once daily	
Subject analysis set title	Doravirine 100 mg: Part I
Subject analysis set type	Safety analysis
Subject analysis set description:	
Doravirine (MK-1439) 100 mg once daily plus TRUVADA once daily	
Subject analysis set title	Doravirine 200 mg: Part I

Subject analysis set type	Safety analysis
Subject analysis set description:	
Doravirine (MK-1439) 200 mg once daily plus TRUVADA once daily	
Subject analysis set title	Efavirenz 600 mg: Part I
Subject analysis set type	Safety analysis
Subject analysis set description:	
Efavirenz 600 mg once daily plus TRUVADA once daily	
Subject analysis set title	Doravirine 25 mg: PartI/II Combined
Subject analysis set type	Safety analysis
Subject analysis set description:	
Doravirine (MK-1439) 25 mg once daily plus TRUVADA once daily	
Subject analysis set title	Doravirine 50 mg: Part I/II Combined
Subject analysis set type	Safety analysis
Subject analysis set description:	
Doravirine (MK-1439) 50 mg once daily plus TRUVADA once daily	
Subject analysis set title	Doravirine 100 mg: Part I/II Combined
Subject analysis set type	Safety analysis
Subject analysis set description:	
Doravirine (MK-1439) 100 mg once daily plus TRUVADA once daily	
Subject analysis set title	Doravirine 200 mg: Part I/II Combined
Subject analysis set type	Safety analysis
Subject analysis set description:	
Doravirine (MK-1439) 200 mg once daily plus TRUVADA once daily	
Subject analysis set title	Efavirenz 600 mg: Part I/II Combined
Subject analysis set type	Safety analysis
Subject analysis set description:	
Efavirenz 600 mg once daily plus TRUVADA once daily	

Reporting group values	Doravirine 25 mg: Part I	Doravirine 50 mg: Part I	Doravirine 100 mg: Part I
Number of subjects	40	43	42
Age Categorical			
Two randomised participants who were enrolled in the overall population (n=342) never received treatment.			
Units: Subjects			
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)	38	42	41
From 65-84 years	2	1	1
85 years and over	0	0	0
Age Continuous			
Two enrolled participants in the overall population who were randomized (n=342) never received treatment.			
Units: years			
arithmetic mean	38.9	38.3	36.5
full range (min-max)	21 to 69	25 to 66	19 to 67

Gender Categorical Units: Subjects			
Female	38	37	36
Male	2	6	6

Reporting group values	Doravirine 200 mg: Part I	Efavirenz 600 mg: Part I	Doravirine 25 mg: PartI/II Combined
Number of subjects	41	42	40
Age Categorical			
Two randomised participants who were enrolled in the overall population (n=342) never received treatment.			
Units: Subjects			
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)	41	42	38
From 65-84 years	0	0	2
85 years and over	0	0	0
Age Continuous			
Two enrolled participants in the overall population who were randomized (n=342) never received treatment.			
Units: years			
arithmetic mean	34.4	35	38.9
full range (min-max)	23 to 50	22 to 54	21 to 69
Gender Categorical Units: Subjects			
Female	40	38	38
Male	1	4	2

Reporting group values	Doravirine 50 mg: Part I/II Combined	Doravirine 100 mg: Part I/II Combined	Doravirine 200 mg: Part I/II Combined
Number of subjects	43	108	41
Age Categorical			
Two randomised participants who were enrolled in the overall population (n=342) never received treatment.			
Units: Subjects			
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)	42	107	41
From 65-84 years	1	1	0
85 years and over	0	0	0
Age Continuous			
Two enrolled participants in the overall population who were randomized (n=342) never received treatment.			

Units: years			
arithmetic mean	38.3	36.8	34.4
full range (min-max)	25 to 66	19 to 67	21 to 50
Gender Categorical			
Units: Subjects			
Female	37	99	40
Male	6	9	1

Reporting group values	Efavirenz 600 mg: Part I/II Combined		
Number of subjects	108		
Age Categorical			
Two randomised participants who were enrolled in the overall population (n=342) never received treatment.			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	108		
From 65-84 years	0		
85 years and over	0		
Age Continuous			
Two enrolled participants in the overall population who were randomized (n=342) never received treatment.			
Units: years			
arithmetic mean	35.2		
full range (min-max)	20 to 57		
Gender Categorical			
Units: Subjects			
Female	101		
Male	7		

End points

End points reporting groups

Reporting group title	Doravirine 25 mg: Part I
Reporting group description: Doravirine (MK-1439) 25 mg once daily plus TRUVADA once daily	
Reporting group title	Doravirine 50 mg: Part I
Reporting group description: Doravirine (MK-1439) 50 mg once daily plus TRUVADA once daily	
Reporting group title	Doravirine 100 mg: Part I
Reporting group description: Doravirine (MK-1439) 100 mg once daily plus TRUVADA once daily	
Reporting group title	Doravirine 200 mg: Part I
Reporting group description: Doravirine (MK-1439) 200 mg once daily plus TRUVADA once daily	
Reporting group title	Efavirenz 600 mg: Part I
Reporting group description: Efavirenz 600 mg once daily plus TRUVADA once daily	
Reporting group title	Doravirine 100 mg: Part II
Reporting group description: Doravirine (MK-1439) 100 mg once daily plus TRUVADA once daily	
Reporting group title	Efavirenz 600 mg: Part II
Reporting group description: Efavirenz 600 mg once daily plus TRUVADA once daily	
Subject analysis set title	Doravirine 25 mg: Part I
Subject analysis set type	Safety analysis
Subject analysis set description: Doravirine (MK-1439) 25 mg once daily plus TRUVADA once daily	
Subject analysis set title	Doravirine 50 mg: Part I
Subject analysis set type	Safety analysis
Subject analysis set description: Doravirine (MK-1439) 50 mg once daily plus TRUVADA once daily	
Subject analysis set title	Doravirine 100 mg: Part I
Subject analysis set type	Safety analysis
Subject analysis set description: Doravirine (MK-1439) 100 mg once daily plus TRUVADA once daily	
Subject analysis set title	Doravirine 200 mg: Part I
Subject analysis set type	Safety analysis
Subject analysis set description: Doravirine (MK-1439) 200 mg once daily plus TRUVADA once daily	
Subject analysis set title	Efavirenz 600 mg: Part I
Subject analysis set type	Safety analysis
Subject analysis set description: Efavirenz 600 mg once daily plus TRUVADA once daily	
Subject analysis set title	Doravirine 25 mg: PartI/II Combined
Subject analysis set type	Safety analysis
Subject analysis set description: Doravirine (MK-1439) 25 mg once daily plus TRUVADA once daily	
Subject analysis set title	Doravirine 50 mg: Part I/II Combined
Subject analysis set type	Safety analysis

Subject analysis set description:	
Doravirine (MK-1439) 50 mg once daily plus TRUVADA once daily	
Subject analysis set title	Doravirine 100 mg: Part I/II Combined
Subject analysis set type	Safety analysis
Subject analysis set description:	
Doravirine (MK-1439) 100 mg once daily plus TRUVADA once daily	
Subject analysis set title	Doravirine 200 mg: Part I/II Combined
Subject analysis set type	Safety analysis
Subject analysis set description:	
Doravirine (MK-1439) 200 mg once daily plus TRUVADA once daily	
Subject analysis set title	Efavirenz 600 mg: Part I/II Combined
Subject analysis set type	Safety analysis
Subject analysis set description:	
Efavirenz 600 mg once daily plus TRUVADA once daily	

Primary: Percentage of Participants With At Least 1 Adverse Event (AE) in Weeks 0-24: MK-1439 All Doses vs. Efavirenz (Part I)

End point title	Percentage of Participants With At Least 1 Adverse Event (AE) in Weeks 0-24: MK-1439 All Doses vs. Efavirenz (Part I)
End point description:	
A primary endpoint in Part I was the percentage of participants receiving doravirine (MK-1439) at all doses (25 mg, 50 mg, 100 mg, or 200 mg), compared with participants receiving efavirenz 600 mg, who had at least 1 AE over 24 weeks of treatment. The relative number (n/N [%]) of participants in any treatment group with at least 1 AE was primarily assessed for Weeks 0-24.	
End point type	Primary
End point timeframe:	
Up to Week 24	

End point values	Doravirine 25 mg: Part I	Doravirine 50 mg: Part I	Doravirine 100 mg: Part I	Doravirine 200 mg: Part I
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	40	43	42	41
Units: Percentage of participants				
number (confidence interval 95%)	90 (76.3 to 97.2)	93 (80.9 to 98.5)	71.4 (55.4 to 84.3)	85.4 (70.8 to 94.4)

End point values	Efavirenz 600 mg: Part I			
Subject group type	Subject analysis set			
Number of subjects analysed	42			
Units: Percentage of participants				
number (confidence interval 95%)	83.3 (68.6 to 93)			

Statistical analyses

Statistical analysis title	Relative % of participants with ≥1 AE
Statistical analysis description: Doravirine minus Efavirenz	
Comparison groups	Doravirine 25 mg: Part I v Efavirenz 600 mg: Part I
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Between-treatment difference
Point estimate	6.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9
upper limit	22.4

Statistical analysis title	Relative % of participants with ≥1 AE
Statistical analysis description: Doravirine minus Efavirenz	
Comparison groups	Doravirine 50 mg: Part I v Efavirenz 600 mg: Part I
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Between-treatment difference
Point estimate	9.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.6
upper limit	24.9

Statistical analysis title	Relative % of participants with ≥1 AE
Statistical analysis description: Doravirine minus Efavirenz	
Comparison groups	Doravirine 100 mg: Part I v Efavirenz 600 mg: Part I
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Between-treatment difference
Point estimate	-11.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.7
upper limit	6.3

Statistical analysis title	Relative % of participants with ≥1 AE
Statistical analysis description:	
Doravirine minus Efavirenz	
Comparison groups	Doravirine 200 mg: Part I v Efavirenz 600 mg: Part I
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Between-treatment difference
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.5
upper limit	18.4

Primary: Percentage of Participants with At Least 1 AE in Weeks 0-24: MK-1439 Selected Dose (100 mg) vs. Efavirenz (Part I & Part II Combined)

End point title	Percentage of Participants with At Least 1 AE in Weeks 0-24: MK-1439 Selected Dose (100 mg) vs. Efavirenz (Part I & Part II Combined)
End point description:	
A primary endpoint in Part I/II combined was the percentage of participants receiving doravirine (MK-1439) at the selected dose (100 mg), compared with participants receiving efavirenz 600 mg, who had at least 1 AE over 24 weeks of treatment. The relative number (n/N [%]) of participants in either treatment group with ≥1 AE was primarily assessed for Weeks 0-24.	
End point type	Primary
End point timeframe:	
Up to Week 24	

End point values	Doravirine 100 mg: Part I/II Combined	Efavirenz 600 mg: Part I/II Combined		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	108	108		
Units: percentage of participants				
number (confidence interval 95%)	75 (65.7 to 82.8)	85.2 (77.1 to 91.3)		

Statistical analyses

Statistical analysis title	Relative % of participants with ≥1 AE
Statistical analysis description:	
Doravirine minus Eftavirenz	

Comparison groups	Doravirine 100 mg: Part I/II Combined v Efavirenz 600 mg: Part I/II Combined
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Between-treatment difference
Point estimate	-10.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.9
upper limit	0.5

Primary: Percentage of Participants Who Discontinued Study Therapy Due to AEs in Weeks 0-24: MK-1439 All Doses vs. Efavirenz (Part I)

End point title	Percentage of Participants Who Discontinued Study Therapy Due to AEs in Weeks 0-24: MK-1439 All Doses vs. Efavirenz (Part I)

End point description:

A primary endpoint in Part I was the percentage of participants receiving doravirine (MK-1439) at all doses (25 mg, 50 mg, 100 mg, or 200 mg), compared with participants receiving efavirenz 600 mg, who discontinued study therapy due to AEs. The relative number (n/N [%]) of participants who discontinued due to AEs was primarily assessed for Weeks 0-24.

End point type	Primary

End point timeframe:

Up to Week 24

End point values	Doravirine 25 mg: Part I	Doravirine 50 mg: Part I	Doravirine 100 mg: Part I	Doravirine 200 mg: Part I
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	40	43	42	41
Units: Percentage of participants				
number (confidence interval 95%)	2.5 (0.1 to 13.2)	7 (1.5 to 19.1)	2.4 (0.1 to 12.6)	0 (0 to 8.6)

End point values	Efavirenz 600 mg: Part I			
Subject group type	Subject analysis set			
Number of subjects analysed	42			
Units: Percentage of participants				
number (confidence interval 95%)	4.8 (0.6 to 16.2)			

Statistical analyses

Statistical analysis title	Relative % of participants discontinued for AEs
Statistical analysis description: Doravirine minus Efavirenz	
Comparison groups	Doravirine 25 mg: Part I v Efavirenz 600 mg: Part I
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Between-treatment difference
Point estimate	-2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.7
upper limit	8.8

Statistical analysis title	Relative % of participants discontinued for AEs
Statistical analysis description: Doravirine minus Efavirenz	
Comparison groups	Doravirine 50 mg: Part I v Efavirenz 600 mg: Part I
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Between-treatment difference
Point estimate	2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.9
upper limit	14.7

Statistical analysis title	Relative % of participants discontinued for AEs
Statistical analysis description: Doravirine minus Efavirenz	
Comparison groups	Doravirine 100 mg: Part I v Efavirenz 600 mg: Part I
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Between-treatment difference
Point estimate	-2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.8
upper limit	8.2

Statistical analysis title	Relative % of participants discontinued for AEs
Statistical analysis description: Doravirine minus Efavirenz	
Comparison groups	Doravirine 200 mg: Part I v Efavirenz 600 mg: Part I
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Between-treatment difference
Point estimate	-4.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.9
upper limit	4.1

Primary: Percentage of Participants with Central Nervous System (CNS) Events by Week 8: MK-1439 Selected Dose (100 mg) vs. Efavirenz (Part I & Part II Combined)	
End point title	Percentage of Participants with Central Nervous System (CNS) Events by Week 8: MK-1439 Selected Dose (100 mg) vs. Efavirenz (Part I & Part II Combined)
End point description: A key primary endpoint in Part I/II combined was the percentage of participants receiving doravirine (MK-1439) at the selected dose (100 mg), compared with participants receiving efavirenz 600 mg, who had CNS Events over 8 weeks of treatment. Although 24 individual CNS events were described, they were pooled and evaluated as CNS events. The relative number (n/N [%]) of participants in either treatment group with CNS events was primarily assessed for Week 8.	
End point type	Primary
End point timeframe: Up to Week 8	

End point values	Doravirine 100 mg: Part I/II Combined	Efavirenz 600 mg: Part I/II Combined		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	108	108		
Units: Percentage of participants				
number (confidence interval 95%)	24.1 (16.4 to 33.3)	44.4 (34.9 to 54.3)		

Statistical analyses

Statistical analysis title	Relative % of participants with CNS events

Statistical analysis description:	
Doravirine minus Efavirenz	
Comparison groups	Doravirine 100 mg: Part I/II Combined v Efavirenz 600 mg: Part I/II Combined
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Miettinen and Nurminen method
Parameter estimate	Between-treatment difference
Point estimate	-20.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-32.4
upper limit	-7.8

Primary: Percentage of Participants with CNS Events by Week 24: MK-1439 Selected Dose (100 mg) vs. Efavirenz (Part I & Part II Combined)

End point title	Percentage of Participants with CNS Events by Week 24: MK-1439 Selected Dose (100 mg) vs. Efavirenz (Part I & Part II Combined)
End point description:	
A key primary endpoint in Part I/II combined was the percentage of participants receiving doravirine (MK-1439) at the selected dose (100 mg), compared with participants receiving efavirenz 600 mg, who had CNS events over 24 weeks of treatment. Although 24 individual CNS AEs were described, they were pooled and evaluated as CNS events. The relative number (n/N [%]) of participants in either treatment group with CNS AEs was primarily assessed for Week 24.	
End point type	Primary
End point timeframe:	
Up to Week 24	

End point values	Doravirine 100 mg: Part I/II Combined	Efavirenz 600 mg: Part I/II Combined		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	108	108		
Units: Percentage of participants				
number (confidence interval 95%)	26.9 (18.8 to 36.2)	47.2 (37.5 to 57.1)		

Statistical analyses

Statistical analysis title	Relative % of participants with CNS events
Statistical analysis description:	
Doravirine minus Efavirenz	
Comparison groups	Doravirine 100 mg: Part I/II Combined v Efavirenz 600 mg:

	Part I/II Combined
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Miettinen and Nurminen method
Parameter estimate	Between-treatment difference
Point estimate	-20.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-32.6
upper limit	-7.5

Primary: Percentage of Participants with Virologic Response (plasma HIV RNA < 40 copies/mL) at Week 24: MK-1439 All Doses vs. Efavirenz (Part I)

End point title	Percentage of Participants with Virologic Response (plasma HIV RNA < 40 copies/mL) at Week 24: MK-1439 All Doses vs. Efavirenz (Part I)

End point description:

A primary endpoint in Part I was the percentage of participants receiving doravirine (MK-1439) at all doses (25 mg, 50 mg, 100 mg, or 200 mg), compared with participants receiving efavirenz 600 mg, who had a virologic response (plasma HIV RNA < 40 copies/mL) over 24 weeks of treatment. The relative number (n/N [%]) of participants in any treatment group with a virologic response was primarily assessed for Weeks 0-24. The Non-Completer = Failure (NC=F) approach, in which participants who prematurely discontinued assigned treatment for any reason and were considered as failures thereafter, was used as the primary approach to handle missing data this analysis of efficacy.

End point type	Primary

End point timeframe:

Week 24

End point values	Doravirine 25 mg: Part I	Doravirine 50 mg: Part I	Doravirine 100 mg: Part I	Doravirine 200 mg: Part I
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	40	43	42	41
Units: Percentage of participants				
number (confidence interval 95%)	80 (64.4 to 90.9)	74.4 (58.8 to 86.5)	71.4 (55.4 to 84.3)	80.5 (65.1 to 91.2)

End point values	Efavirenz 600 mg: Part I			
Subject group type	Subject analysis set			
Number of subjects analysed	42			
Units: Percentage of participants				
number (confidence interval 95%)	64.3 (48 to 78.4)			

Statistical analyses

Statistical analysis title	Relative % with Virologic Response
Statistical analysis description: Doravirine minus Efavirenz	
Comparison groups	Doravirine 25 mg: Part I v Efavirenz 600 mg: Part I
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Between-treatment difference
Point estimate	15.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.1
upper limit	34.4

Statistical analysis title	Relative % with Virologic Response
Statistical analysis description: Doravirine minus Efavirenz	
Comparison groups	Doravirine 50 mg: Part I v Efavirenz 600 mg: Part I
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Between-treatment difference
Point estimate	10
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.6
upper limit	29.1

Statistical analysis title	Relative % with Virologic Response
Statistical analysis description: Doravirine minus Efavirenz	
Comparison groups	Doravirine 100 mg: Part I v Efavirenz 600 mg: Part I

Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Between-treatment difference
Point estimate	6.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.2
upper limit	26

Statistical analysis title	Relative % with Virologic Response
Statistical analysis description:	
Doravirine minus Efavirenz	
Comparison groups	Doravirine 200 mg: Part I v Efavirenz 600 mg: Part I
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Between-treatment difference
Point estimate	15.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	34.4

Primary: Percentage of Participants with Virologic Response (plasma HIV RNA < 40 copies/mL) at Week 24: MK-1439 Selected Dose (100 mg) vs. Efavirenz (Part I & Part II Combined)

End point title	Percentage of Participants with Virologic Response (plasma HIV RNA < 40 copies/mL) at Week 24: MK-1439 Selected Dose (100 mg) vs. Efavirenz (Part I & Part II Combined)

End point description:

A primary endpoint in Part I/II combined was the percentage of participants receiving doravirine (MK-1439) at the selected dose (100 mg), compared with participants receiving efavirenz 600 mg, who had a virologic response (plasma HIV RNA < 40 copies/mL) over 24 weeks of treatment. The relative number (n/N [%]) of participants in either treatment group with this virologic response was primarily assessed for Weeks 0-24. The NC=F approach was used as the primary approach to handle missing data this analysis of efficacy.

End point type	Primary

End point timeframe:

Week 24

End point values	Doravirine 100 mg: Part I/II Combined	Efavirenz 600 mg: Part I/II Combined		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	78	79		
Units: Percentage of participants				
number (confidence interval 95%)	72.9 (63.4 to 81)	73.1 (63.8 to 81.2)		

Statistical analyses

Statistical analysis title	Relative % with Virologic Response
Statistical analysis description: Doravirine minus Efavirenz	
Comparison groups	Doravirine 100 mg: Part I/II Combined v Efavirenz 600 mg: Part I/II Combined
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Between-treatment difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.3
upper limit	11.2

Secondary: Percentage of Participants with At Least 1 AE in Weeks 0-48: MK-1439 Selected Dose (100 mg) vs. Efavirenz (Part I & Part II Combined)

End point title	Percentage of Participants with At Least 1 AE in Weeks 0-48: MK-1439 Selected Dose (100 mg) vs. Efavirenz (Part I & Part II Combined)
End point description: A secondary endpoint in Part I/II combined was the percentage of participants receiving doravirine (MK-1439) at the selected dose (100 mg), compared with participants receiving efavirenz 600 mg, who had at least 1 AE over 48 weeks of treatment. The relative number (n/N [%]) of participants in any treatment group with at least 1 AE was primarily assessed for Weeks 0-48.	
End point type	Secondary
End point timeframe: Up to 48 weeks	

End point values	Doravirine 100 mg: Part I/II Combined	Efavirenz 600 mg: Part I/II Combined		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	108	108		
Units: Percentage of participants				
number (confidence interval 95%)	87 (79.2 to 92.7)	89.8 (82.5 to 94.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with At Least 1 AE in Weeks 0-96: MK-1439 Selected Dose (100 mg) vs. Efavirenz (Part I & Part II Combined)

End point title	Percentage of Participants with At Least 1 AE in Weeks 0-96: MK-1439 Selected Dose (100 mg) vs. Efavirenz (Part I & Part II Combined)

End point description:

A secondary endpoint in Part I/II combined was the percentage of participants receiving doravirine (MK-1439) at the selected dose (100 mg), compared with participants receiving efavirenz 600 mg, who had at least 1 AE was primarily assessed for Weeks 0-96, plus a 14-day post-treatment follow-up period.

End point type	Secondary

End point timeframe:

Up to 98 weeks

End point values	Doravirine 100 mg: Part I/II Combined	Efavirenz 600 mg: Part I/II Combined		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	108	108		
Units: Percentage of participants				
number (confidence interval 95%)	89.8 (82.5 to 94.8)	96.3 (90.8 to 99)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Virologic Response (plasma HIV RNA < 200 copies/mL) at Week 24: MK-1439 All Doses vs. Efavirenz (Part I)

End point title	Percentage of Participants with Virologic Response (plasma HIV RNA < 200 copies/mL) at Week 24: MK-1439 All Doses vs. Efavirenz (Part I)

End point description:

A secondary endpoint in Part I was the percentage of participants receiving doravirine (MK-1439) at all doses (25 mg, 50 mg, 100 mg, and 200 mg), compared with participants receiving efavirenz 600 mg, who had a virologic response (plasma HIV RNA < 200 copies/mL) over 24 weeks of treatment. The relative number (n/N [%]) of participants in either treatment group with this virologic response was

assessed for Weeks 0-24. The NC=F approach was used as the primary approach to handle missing data this analysis of efficacy.

End point type	Secondary

End point timeframe:

Up to Week 24

End point values	Doravirine 25 mg: Part I	Doravirine 50 mg: Part I	Doravirine 100 mg: Part I	Doravirine 200 mg: Part I
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	40	43	42	41
Units: Percentage of participants				
number (confidence interval 95%)	85 (70.2 to 94.3)	83.7 (69.3 to 93.2)	92.9 (80.5 to 98.5)	90.2 (76.9 to 97.3)

End point values	Efavirenz 600 mg: Part I			
Subject group type	Subject analysis set			
Number of subjects analysed	42			
Units: Percentage of participants				
number (confidence interval 95%)	81 (65.9 to 91.4)			

Statistical analyses

Statistical analysis title	Relative % with Virologic Response
Statistical analysis description:	
Doravirine minus Efavirenz	
Comparison groups	Doravirine 25 mg: Part I v Efavirenz 600 mg: Part I
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Between-treatment difference
Point estimate	4.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.5
upper limit	21.5

Statistical analysis title	Relative % with Virologic Response
Statistical analysis description:	
Doravirine minus Efavirenz	
Comparison groups	Doravirine 50 mg: Part I v Efavirenz 600 mg: Part I

Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Between-treatment difference
Point estimate	2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.9
upper limit	19.8

Statistical analysis title	Relative % with Virologic Response
Statistical analysis description: Doravirine minus Efavirenz	
Comparison groups	Doravirine 100 mg: Part I v Efavirenz 600 mg: Part I
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Between-treatment difference
Point estimate	12.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	28

Statistical analysis title	Relative % with Virologic Response
Statistical analysis description: Doravirine minus Efavirenz	
Comparison groups	Doravirine 200 mg: Part I v Efavirenz 600 mg: Part I
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Between-treatment difference
Point estimate	9.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.2
upper limit	25.7

Secondary: Change from Baseline in Cluster of Differentiation 4 (CD4) T Lymphocyte Cell Count at Week 24: MK-1439 All Doses vs. Efavirenz (Part I)

End point title	Change from Baseline in Cluster of Differentiation 4 (CD4) T

	Lymphocyte Cell Count at Week 24: MK-1439 All Doses vs. Efavirenz (Part I)

End point description:

A secondary endpoint in Part I was the change from baseline in the CD4 cell count at Week 24 in participants receiving doravirine (MK-1439) at all doses (25 mg, 50 mg, 100 mg, and 200 mg), compared with participants receiving efavirenz 600 mg. The Observed Failure (OF) approach was used to handle missing data, and the Baseline CD4 cell count was carried forward for subjects who discontinued assigned treatment due to lack of efficacy.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Doravirine 25 mg: Part I	Doravirine 50 mg: Part I	Doravirine 100 mg: Part I	Doravirine 200 mg: Part I
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	38	41	41	40
Units: cells/mm3				
arithmetic mean (confidence interval 95%)	154.1 (115.1 to 193.1)	112.9 (74.5 to 151.2)	133.6 (100.4 to 166.8)	140.7 (95.6 to 185.7)

End point values	Efavirenz 600 mg: Part I			
Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: cells/mm3				
arithmetic mean (confidence interval 95%)	121.1 (73.3 to 169)			

Statistical analyses

Statistical analysis title	Difference in CD4 Changes from Baseline
Statistical analysis description:	
Doravirine minus Efavirenz	
Comparison groups	Doravirine 25 mg: Part I v Efavirenz 600 mg: Part I
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Between-treatment difference
Point estimate	33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.1
upper limit	94

Statistical analysis title	Difference in CD4 Changes from Baseline
Comparison groups	Doravirine 50 mg: Part I v Efavirenz 600 mg: Part I
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Between-treatment difference
Point estimate	-8.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-68.5
upper limit	51.9

Statistical analysis title	Difference in CD4 Changes from Baseline
Statistical analysis description: Doravirine minus Eftavirenz	
Comparison groups	Doravirine 100 mg: Part I v Efavirenz 600 mg: Part I
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Between-treatment difference
Point estimate	12.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-44.6
upper limit	69.5

Statistical analysis title	Difference in CD4 Changes from Baseline
Comparison groups	Doravirine 200 mg: Part I v Efavirenz 600 mg: Part I
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Between-treatment difference
Point estimate	19.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-45.1
upper limit	84.2

Secondary: Change from Baseline in CD4 Cell Count at Week 24: MK-1439 Selected Dose (100 mg) vs. Efavirenz (Part I & Part II Combined)

End point title	Change from Baseline in CD4 Cell Count at Week 24: MK-1439 Selected Dose (100 mg) vs. Efavirenz (Part I & Part II Combined)

End point description:

A secondary objective in Part I/II combined was to assess the change from baseline in the CD4 cell count at Week 24 in participants receiving doravirine (MK-1439) at the selected dose (100 mg), compared with participants receiving efavirenz 600 mg. The OF approach was used to handle missing data, and the Baseline CD4 cell count was carried forward for subjects who discontinued assigned therapy due to lack of efficacy.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Doravirine 100 mg: Part I/II Combined	Efavirenz 600 mg: Part I/II Combined		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	106	101		
Units: cells/mm3				
arithmetic mean (confidence interval 95%)	152.3 (121.7 to 182.8)	146 (113.1 to 178.8)		

Statistical analyses

Statistical analysis title	Difference in CD4 Changes from Baseline
Comparison groups	Doravirine 100 mg: Part I/II Combined v Efavirenz 600 mg: Part I/II Combined
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Between-treatment difference
Point estimate	6.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-38.2
upper limit	50.8

Secondary: Percentage of Participants with Virologic Response (plasma HIV RNA < 40 copies/mL) at Week 48: MK-1439 Selected Dose vs. Efavirenz (Part I & Part II Combined)

End point title	Percentage of Participants with Virologic Response (plasma HIV

	RNA < 40 copies/mL) at Week 48: MK-1439 Selected Dose vs. Efavirenz (Part I & Part II Combined)

End point description:

A secondary endpoint in Part I/II combined was the percentage of participants receiving doravirine (MK-1439) at the selected dose (100 mg), compared with participants receiving efavirenz 600 mg, who had a virologic response (plasma HIV RNA < 40 copies/mL) over 48 weeks of treatment. The relative number (n/N [%]) of participants in either treatment group with this virologic response was primarily assessed for Weeks 0-48, using the NC=F approach to handle missing data in this analysis of efficacy.

End point type	Secondary

End point timeframe:

Week 48

End point values	Doravirine 100 mg: Part I/II Combined	Efavirenz 600 mg: Part I/II Combined		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	108	107		
Units: Percentage of participants				
number (confidence interval 95%)	77.8 (68.8 to 85.2)	78.7 (69.8 to 86)		

Statistical analyses

Statistical analysis title	Relative % with Virologic Response
Statistical analysis description:	
Doravirine minus Efavirenz	
Comparison groups	Doravirine 100 mg: Part I/II Combined v Efavirenz 600 mg: Part I/II Combined
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Between-treatment difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.2
upper limit	10

Secondary: Change from Baseline in CD4 Cell Count at Week 48: MK-1439 Selected Dose (100 mg) vs. Efavirenz (Part I & Part II Combined)

End point title	Change from Baseline in CD4 Cell Count at Week 48: MK-1439 Selected Dose (100 mg) vs. Efavirenz (Part I & Part II Combined)

End point description:

A secondary endpoint in Part I/II combined was the change from baseline in the CD4 count at Week 48 in participants receiving doravirine (MK-1439) at the selected dose (100 mg), compared with participants receiving efavirenz 600 mg. The OF approach was used to handle missing data, and the

Baseline CD4 cell count was carried forward for subjects who discontinued assigned therapy due to lack of efficacy.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	Doravirine 100 mg: Part I/II Combined	Efavirenz 600 mg: Part I/II Combined		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	102	100		
Units: cells/mm3				
arithmetic mean (confidence interval 95%)	191.9 (160.8 to 223.1)	194.5 (163.2 to 225.9)		

Statistical analyses

Statistical analysis title	Difference in CD4 Changes from Baseline

Statistical analysis description:

Doravirine minus Efavirenz

Comparison groups	Doravirine 100 mg: Part I/II Combined v Efavirenz 600 mg: Part I/II Combined
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Between-treatment difference
Point estimate	-2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-46.5
upper limit	41.3

Secondary: Percentage of Participants with Virologic Response (plasma HIV RNA < 40 copies/mL) at Week 96: MK-1439 Selected Dose (100 mg) vs. Efavirenz (Part I & Part II Combined)

End point title	Percentage of Participants with Virologic Response (plasma HIV RNA < 40 copies/mL) at Week 96: MK-1439 Selected Dose (100 mg) vs. Efavirenz (Part I & Part II Combined)

End point description:

A secondary endpoint in Part I/II combined was the percentage of participants receiving doravirine (MK-1439) at the selected dose (100 mg), compared with participants receiving efavirenz 600 mg, who had a virologic response (plasma HIV RNA < 40 copies/mL) over 96 weeks of treatment. The relative number (n/N [%]) of participants in either treatment group with this virologic response was primarily assessed for Weeks 0-96, using the NC=F approach to handle missing data in this analysis of efficacy.

End point type	Secondary

End point timeframe:

Week 96

End point values	Doravirine 100 mg: Part I/II Combined	Efavirenz 600 mg: Part I/II Combined		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	81	82		
Units: Percentage of participants				
number (confidence interval 95%)	75 (65.7 to 82.8)	75.9 (66.7 to 83.6)		

Statistical analyses

Statistical analysis title	Relative % with Virologic Response
Comparison groups	Doravirine 100 mg: Part I/II Combined v Efavirenz 600 mg: Part I/II Combined
Number of subjects included in analysis	163
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Between-treatment difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.4
upper limit	10.7

Secondary: Change from Baseline in CD4 Cell Count at Week 96: MK-1439 Selected Dose (100 mg) vs. Efavirenz (Part I & Part II Combined)

End point title	Change from Baseline in CD4 Cell Count at Week 96: MK-1439 Selected Dose (100 mg) vs. Efavirenz (Part I & Part II Combined)

End point description:

A secondary endpoint in Part I/II combined was the change from baseline in the CD4 count at Week 96 in participants receiving doravirine (MK-1439) at the selected dose (100 mg), compared with participants receiving efavirenz 600 mg. The OF approach was used to handle missing data, and the Baseline CD4 cell count was carried forward for subjects who discontinued assigned therapy due to lack of efficacy.

End point type	Secondary

End point timeframe:

Baseline, Week 96

End point values	Doravirine 100 mg: Part I/II Combined	Efavirenz 600 mg: Part I/II Combined		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	95	93		
Units: cells/mm3				
arithmetic mean (confidence interval 95%)	259.2 (220 to 298.3)	263.6 (218.1 to 309.1)		

Statistical analyses

Statistical analysis title	Difference in CD4 Changes from Baseline
Statistical analysis description: Doravirine minus Efavirenz	
Comparison groups	Doravirine 100 mg: Part I/II Combined v Efavirenz 600 mg: Part I/II Combined
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Between-treatment difference
Point estimate	-4.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-64
upper limit	55.1

Secondary: Percentage of Participants with Virologic Response (plasma HIV RNA < 200 copies/mL) at Week 48: MK-1439 Selected Dose (100 mg) vs. Efavirenz (Part I & Part II Combined)

End point title	Percentage of Participants with Virologic Response (plasma HIV RNA < 200 copies/mL) at Week 48: MK-1439 Selected Dose (100 mg) vs. Efavirenz (Part I & Part II Combined)

End point description:

A secondary endpoint in Part I/II combined was the percentage of participants receiving doravirine (MK-1439) at the selected dose (100 mg), compared with participants receiving efavirenz 600 mg, who had a virologic response (plasma HIV RNA < 200 copies/mL) over 48 weeks of treatment. The relative number (n/N [%]) of participants in either treatment group with this virologic response was primarily assessed for Weeks 0-48, using the NC=F approach to handle missing data in this analysis of efficacy.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	Doravirine 100 mg: Part I/II Combined	Efavirenz 600 mg: Part I/II Combined		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	108	107		
Units: Percentage of participants				
number (confidence interval 95%)	85.2 (77.1 to 91.3)	85 (76.9 to 91.2)		

Statistical analyses

Statistical analysis title	Relative % with Virologic Response
Statistical analysis description: Doravirine minus Efavirenz	
Comparison groups	Doravirine 100 mg: Part I/II Combined v Efavirenz 600 mg: Part I/II Combined
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Between-treatment difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.7
upper limit	9.9

Secondary: Percentage of Participants with Virologic Response (plasma HIV RNA < 200 copies/mL) at Week 96: MK-1439 Selected Dose (100 mg) vs. Efavirenz (Part I & Part II Combined)

End point title	Percentage of Participants with Virologic Response (plasma HIV RNA < 200 copies/mL) at Week 96: MK-1439 Selected Dose (100 mg) vs. Efavirenz (Part I & Part II Combined)

End point description:

A secondary endpoint in Part I/II combined was the percentage of participants receiving doravirine (MK-1439) at the selected dose (100 mg), compared with participants receiving efavirenz 600 mg, who had a virologic response (plasma HIV RNA < 200 copies/mL) over 96 weeks of treatment. The relative number (n/N [%]) of participants in either treatment group with this virologic response was primarily assessed for Weeks 0-96, using the NC=F approach to handle missing data in this analysis of efficacy.

End point type	Secondary

End point timeframe:

Up to Week 96

End point values	Doravirine 100 mg: Part I/II Combined	Efavirenz 600 mg: Part I/II Combined		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	108	107		
Units: Percentage of participants				
number (confidence interval 95%)	79.6 (70.8 to 86.8)	75.9 (66.7 to 83.6)		

Statistical analyses

Statistical analysis title	Relative % with Virologic Response
Statistical analysis description: Doravirine minus Efavirenz	
Comparison groups	Doravirine 100 mg: Part I/II Combined v Efavirenz 600 mg: Part I/II Combined
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Between-treatment difference
Point estimate	3.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.3
upper limit	15

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 98 weeks	
Adverse event reporting additional description:	
An AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the SPONSOR's product, whether or not considered related to the use of the product.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups	
Reporting group title	Doravirine 25 mg (n=40)
Reporting group description:	
Doravirine (MK-1439) 25 mg once daily plus TRUVADA once daily	
Reporting group title	Doravirine 50 mg (n=43)
Reporting group description:	
Doravirine (MK-1439) 50 mg once daily plus TRUVADA once daily	
Reporting group title	Doravirine 100 mg (n=108)
Reporting group description:	
Doravirine (MK-1439) 100 mg once daily plus TRUVADA once daily	
Reporting group title	Doravirine 200 mg (n=41)
Reporting group description:	
Doravirine (MK-1439) 200 mg once daily plus TRUVADA once daily	
Reporting group title	Efavirenz 600 mg (n=108)
Reporting group description:	
Efavirenz 600 mg once daily plus TRUVADA once daily	

Serious adverse events	Doravirine 25 mg (n=40)	Doravirine 50 mg (n=43)	Doravirine 100 mg (n=108)
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 40 (10.00%)	1 / 43 (2.33%)	11 / 108 (10.19%)
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)			
B-cell unclassifiable lymphoma high grade			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			

subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hodgkin's disease			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kaposi's sarcoma			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Foreign body			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 108 (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
Jaw fracture			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 108 (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
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiomyopathy			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 108 (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

Pericardial effusion			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 108 (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			
Dizziness			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 108 (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
Headache			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 108 (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
Peroneal nerve palsy			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 108 (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
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biliary dyskinesia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 108 (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
Cholecystitis			

subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	1 / 40 (2.50%)	0 / 43 (0.00%)	0 / 108 (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
Hepatitis toxic			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 108 (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			
Bipolar I disorder			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 108 (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
Drug abuse			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal and connective tissue disorders			
Costochondritis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 108 (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			
Abdominal abscess			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 108 (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
Acute hepatitis C			
subjects affected / exposed	1 / 40 (2.50%)	0 / 43 (0.00%)	0 / 108 (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
Cellulitis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 43 (0.00%)	0 / 108 (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
Cryptosporidiosis infection			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 108 (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
Diverticulitis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 108 (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
Gastroenteritis shigella			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis C			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 108 (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

Pharyngotonsillitis			
subjects affected / exposed	0 / 40 (0.00%)	1 / 43 (2.33%)	0 / 108 (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
Pneumonia			
subjects affected / exposed	1 / 40 (2.50%)	0 / 43 (0.00%)	0 / 108 (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
Sinusitis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 108 (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	Doravirine 200 mg (n=41)	Efavirenz 600 mg (n=108)	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 41 (7.32%)	13 / 108 (12.04%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell unclassifiable lymphoma high grade			
subjects affected / exposed	0 / 41 (0.00%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	0 / 41 (0.00%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hodgkin's disease			
subjects affected / exposed	0 / 41 (0.00%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kaposi's sarcoma			

subjects affected / exposed	0 / 41 (0.00%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Foreign body			
subjects affected / exposed	0 / 41 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaw fracture			
subjects affected / exposed	0 / 41 (0.00%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	0 / 41 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiomyopathy			
subjects affected / exposed	1 / 41 (2.44%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	1 / 41 (2.44%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Dizziness			

subjects affected / exposed	0 / 41 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 41 (0.00%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peroneal nerve palsy			
subjects affected / exposed	0 / 41 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 41 (0.00%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Biliary dyskinesia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	0 / 41 (0.00%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	0 / 41 (0.00%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis toxic			

subjects affected / exposed	0 / 41 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 41 (2.44%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Bipolar I disorder			
subjects affected / exposed	0 / 41 (0.00%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 41 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug abuse			
subjects affected / exposed	0 / 41 (0.00%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	0 / 41 (0.00%)	2 / 108 (1.85%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Costochondritis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			

subjects affected / exposed	0 / 41 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute hepatitis C			
subjects affected / exposed	0 / 41 (0.00%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 41 (0.00%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cryptosporidiosis infection			
subjects affected / exposed	1 / 41 (2.44%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis shigella			
subjects affected / exposed	0 / 41 (0.00%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis C			
subjects affected / exposed	0 / 41 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngotonsillitis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	1 / 41 (2.44%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 108 (0.93%)	
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	Doravirine 25 mg (n=40)	Doravirine 50 mg (n=43)	Doravirine 100 mg (n=108)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 40 (77.50%)	35 / 43 (81.40%)	78 / 108 (72.22%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	0 / 40 (0.00%)	1 / 43 (2.33%)	4 / 108 (3.70%)
occurrences (all)	0	1	5
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	4 / 40 (10.00%)	1 / 43 (2.33%)	4 / 108 (3.70%)
occurrences (all)	4	3	5
Nervous system disorders			
Dizziness			
subjects affected / exposed	5 / 40 (12.50%)	5 / 43 (11.63%)	16 / 108 (14.81%)
occurrences (all)	5	6	17
Headache			
subjects affected / exposed	5 / 40 (12.50%)	6 / 43 (13.95%)	13 / 108 (12.04%)
occurrences (all)	6	8	27
Somnolence			
subjects affected / exposed	3 / 40 (7.50%)	0 / 43 (0.00%)	1 / 108 (0.93%)
occurrences (all)	3	0	1
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed	7 / 40 (17.50%)	5 / 43 (11.63%)	6 / 108 (5.56%)
occurrences (all)	7	7	9
Pyrexia			
subjects affected / exposed	1 / 40 (2.50%)	1 / 43 (2.33%)	6 / 108 (5.56%)
occurrences (all)	1	1	7
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	3 / 40 (7.50%)	0 / 43 (0.00%)	0 / 108 (0.00%)
occurrences (all)	3	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 40 (7.50%)	3 / 43 (6.98%)	5 / 108 (4.63%)
occurrences (all)	3	3	5
Abdominal pain upper			
subjects affected / exposed	1 / 40 (2.50%)	3 / 43 (6.98%)	4 / 108 (3.70%)
occurrences (all)	2	3	5
Constipation			
subjects affected / exposed	2 / 40 (5.00%)	4 / 43 (9.30%)	2 / 108 (1.85%)
occurrences (all)	2	4	2
Diarrhoea			
subjects affected / exposed	10 / 40 (25.00%)	4 / 43 (9.30%)	16 / 108 (14.81%)
occurrences (all)	10	4	18
Haemorrhoids			
subjects affected / exposed	1 / 40 (2.50%)	1 / 43 (2.33%)	4 / 108 (3.70%)
occurrences (all)	1	1	4
Nausea			
subjects affected / exposed	3 / 40 (7.50%)	7 / 43 (16.28%)	13 / 108 (12.04%)
occurrences (all)	3	8	16
Vomiting			
subjects affected / exposed	4 / 40 (10.00%)	1 / 43 (2.33%)	6 / 108 (5.56%)
occurrences (all)	4	1	7
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	2 / 40 (5.00%)	0 / 43 (0.00%)	0 / 108 (0.00%)
occurrences (all)	5	0	0
Cough			

subjects affected / exposed	3 / 40 (7.50%)	1 / 43 (2.33%)	3 / 108 (2.78%)
occurrences (all)	7	1	4
Dyspnoea			
subjects affected / exposed	3 / 40 (7.50%)	0 / 43 (0.00%)	0 / 108 (0.00%)
occurrences (all)	3	0	0
Nasal congestion			
subjects affected / exposed	1 / 40 (2.50%)	3 / 43 (6.98%)	3 / 108 (2.78%)
occurrences (all)	1	3	3
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	2 / 40 (5.00%)	3 / 43 (6.98%)	2 / 108 (1.85%)
occurrences (all)	2	3	2
Night sweats			
subjects affected / exposed	1 / 40 (2.50%)	0 / 43 (0.00%)	1 / 108 (0.93%)
occurrences (all)	1	0	2
Pruritus			
subjects affected / exposed	0 / 40 (0.00%)	3 / 43 (6.98%)	4 / 108 (3.70%)
occurrences (all)	0	3	4
Rash			
subjects affected / exposed	1 / 40 (2.50%)	3 / 43 (6.98%)	6 / 108 (5.56%)
occurrences (all)	1	6	6
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	5 / 40 (12.50%)	9 / 43 (20.93%)	7 / 108 (6.48%)
occurrences (all)	6	9	9
Anxiety			
subjects affected / exposed	1 / 40 (2.50%)	2 / 43 (4.65%)	3 / 108 (2.78%)
occurrences (all)	1	2	4
Depression			
subjects affected / exposed	1 / 40 (2.50%)	3 / 43 (6.98%)	4 / 108 (3.70%)
occurrences (all)	1	4	4
Insomnia			
subjects affected / exposed	1 / 40 (2.50%)	6 / 43 (13.95%)	10 / 108 (9.26%)
occurrences (all)	1	6	10
Nightmare			

subjects affected / exposed	1 / 40 (2.50%)	1 / 43 (2.33%)	9 / 108 (8.33%)
occurrences (all)	1	1	10
Sleep disorder			
subjects affected / exposed	1 / 40 (2.50%)	2 / 43 (4.65%)	6 / 108 (5.56%)
occurrences (all)	1	2	6
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 40 (5.00%)	2 / 43 (4.65%)	6 / 108 (5.56%)
occurrences (all)	2	2	6
Back pain			
subjects affected / exposed	2 / 40 (5.00%)	5 / 43 (11.63%)	6 / 108 (5.56%)
occurrences (all)	2	7	7
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	1 / 40 (2.50%)	3 / 43 (6.98%)	2 / 108 (1.85%)
occurrences (all)	1	3	2
Bronchitis			
subjects affected / exposed	5 / 40 (12.50%)	3 / 43 (6.98%)	5 / 108 (4.63%)
occurrences (all)	7	5	5
Conjunctivitis			
subjects affected / exposed	1 / 40 (2.50%)	2 / 43 (4.65%)	6 / 108 (5.56%)
occurrences (all)	1	2	7
Gastroenteritis			
subjects affected / exposed	1 / 40 (2.50%)	2 / 43 (4.65%)	9 / 108 (8.33%)
occurrences (all)	2	3	10
Influenza			
subjects affected / exposed	6 / 40 (15.00%)	2 / 43 (4.65%)	3 / 108 (2.78%)
occurrences (all)	9	2	3
Nasopharyngitis			
subjects affected / exposed	3 / 40 (7.50%)	5 / 43 (11.63%)	19 / 108 (17.59%)
occurrences (all)	4	12	31
Oral herpes			
subjects affected / exposed	0 / 40 (0.00%)	1 / 43 (2.33%)	2 / 108 (1.85%)
occurrences (all)	0	1	3
Pharyngitis			

subjects affected / exposed	0 / 40 (0.00%)	5 / 43 (11.63%)	5 / 108 (4.63%)
occurrences (all)	0	5	7
Sinusitis			
subjects affected / exposed	2 / 40 (5.00%)	2 / 43 (4.65%)	5 / 108 (4.63%)
occurrences (all)	2	2	7
Syphilis			
subjects affected / exposed	4 / 40 (10.00%)	1 / 43 (2.33%)	6 / 108 (5.56%)
occurrences (all)	6	2	7
Tinea pedis			
subjects affected / exposed	3 / 40 (7.50%)	0 / 43 (0.00%)	1 / 108 (0.93%)
occurrences (all)	3	0	1
Tonsillitis			
subjects affected / exposed	2 / 40 (5.00%)	1 / 43 (2.33%)	1 / 108 (0.93%)
occurrences (all)	2	1	1
Upper respiratory tract infection			
subjects affected / exposed	4 / 40 (10.00%)	2 / 43 (4.65%)	10 / 108 (9.26%)
occurrences (all)	5	6	14

Non-serious adverse events	Doravirine 200 mg (n=41)	Efavirenz 600 mg (n=108)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 41 (87.80%)	82 / 108 (75.93%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	2 / 41 (4.88%)	6 / 108 (5.56%)	
occurrences (all)	2	6	
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	3 / 41 (7.32%)	5 / 108 (4.63%)	
occurrences (all)	10	6	
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 41 (7.32%)	31 / 108 (28.70%)	
occurrences (all)	3	38	
Headache			
subjects affected / exposed	7 / 41 (17.07%)	15 / 108 (13.89%)	
occurrences (all)	7	26	

Somnolence			
subjects affected / exposed	0 / 41 (0.00%)	1 / 108 (0.93%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	5 / 41 (12.20%)	7 / 108 (6.48%)	
occurrences (all)	7	7	
Pyrexia			
subjects affected / exposed	0 / 41 (0.00%)	3 / 108 (2.78%)	
occurrences (all)	0	4	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 41 (0.00%)	0 / 108 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 41 (0.00%)	4 / 108 (3.70%)	
occurrences (all)	0	4	
Abdominal pain upper			
subjects affected / exposed	2 / 41 (4.88%)	5 / 108 (4.63%)	
occurrences (all)	2	9	
Constipation			
subjects affected / exposed	0 / 41 (0.00%)	4 / 108 (3.70%)	
occurrences (all)	0	4	
Diarrhoea			
subjects affected / exposed	5 / 41 (12.20%)	18 / 108 (16.67%)	
occurrences (all)	5	20	
Haemorrhoids			
subjects affected / exposed	0 / 41 (0.00%)	6 / 108 (5.56%)	
occurrences (all)	0	6	
Nausea			
subjects affected / exposed	9 / 41 (21.95%)	11 / 108 (10.19%)	
occurrences (all)	9	12	
Vomiting			
subjects affected / exposed	1 / 41 (2.44%)	7 / 108 (6.48%)	
occurrences (all)	1	8	

Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	3 / 41 (7.32%)	2 / 108 (1.85%)	
occurrences (all)	3	2	
Cough			
subjects affected / exposed	3 / 41 (7.32%)	6 / 108 (5.56%)	
occurrences (all)	3	10	
Dyspnoea			
subjects affected / exposed	0 / 41 (0.00%)	0 / 108 (0.00%)	
occurrences (all)	0	0	
Nasal congestion			
subjects affected / exposed	0 / 41 (0.00%)	3 / 108 (2.78%)	
occurrences (all)	0	3	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 41 (0.00%)	0 / 108 (0.00%)	
occurrences (all)	0	0	
Night sweats			
subjects affected / exposed	0 / 41 (0.00%)	6 / 108 (5.56%)	
occurrences (all)	0	6	
Pruritus			
subjects affected / exposed	0 / 41 (0.00%)	3 / 108 (2.78%)	
occurrences (all)	0	3	
Rash			
subjects affected / exposed	2 / 41 (4.88%)	9 / 108 (8.33%)	
occurrences (all)	2	10	
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	4 / 41 (9.76%)	19 / 108 (17.59%)	
occurrences (all)	4	21	
Anxiety			
subjects affected / exposed	0 / 41 (0.00%)	6 / 108 (5.56%)	
occurrences (all)	0	9	
Depression			
subjects affected / exposed	0 / 41 (0.00%)	10 / 108 (9.26%)	
occurrences (all)	0	12	

Insomnia			
subjects affected / exposed	3 / 41 (7.32%)	6 / 108 (5.56%)	
occurrences (all)	4	7	
Nightmare			
subjects affected / exposed	0 / 41 (0.00%)	10 / 108 (9.26%)	
occurrences (all)	0	12	
Sleep disorder			
subjects affected / exposed	0 / 41 (0.00%)	8 / 108 (7.41%)	
occurrences (all)	0	11	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 41 (7.32%)	3 / 108 (2.78%)	
occurrences (all)	3	3	
Back pain			
subjects affected / exposed	2 / 41 (4.88%)	10 / 108 (9.26%)	
occurrences (all)	2	14	
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	2 / 41 (4.88%)	1 / 108 (0.93%)	
occurrences (all)	2	2	
Bronchitis			
subjects affected / exposed	5 / 41 (12.20%)	12 / 108 (11.11%)	
occurrences (all)	7	13	
Conjunctivitis			
subjects affected / exposed	0 / 41 (0.00%)	3 / 108 (2.78%)	
occurrences (all)	0	3	
Gastroenteritis			
subjects affected / exposed	2 / 41 (4.88%)	1 / 108 (0.93%)	
occurrences (all)	2	1	
Influenza			
subjects affected / exposed	5 / 41 (12.20%)	2 / 108 (1.85%)	
occurrences (all)	5	2	
Nasopharyngitis			
subjects affected / exposed	12 / 41 (29.27%)	13 / 108 (12.04%)	
occurrences (all)	17	16	
Oral herpes			

subjects affected / exposed	3 / 41 (7.32%)	3 / 108 (2.78%)	
occurrences (all)	3	3	
Pharyngitis			
subjects affected / exposed	2 / 41 (4.88%)	3 / 108 (2.78%)	
occurrences (all)	2	4	
Sinusitis			
subjects affected / exposed	3 / 41 (7.32%)	5 / 108 (4.63%)	
occurrences (all)	4	7	
Syphilis			
subjects affected / exposed	6 / 41 (14.63%)	8 / 108 (7.41%)	
occurrences (all)	7	9	
Tinea pedis			
subjects affected / exposed	0 / 41 (0.00%)	0 / 108 (0.00%)	
occurrences (all)	0	0	
Tonsillitis			
subjects affected / exposed	3 / 41 (7.32%)	4 / 108 (3.70%)	
occurrences (all)	3	4	
Upper respiratory tract infection			
subjects affected / exposed	3 / 41 (7.32%)	13 / 108 (12.04%)	
occurrences (all)	3	19	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 June 2012	The study flow chart, inclusion criteria, and treatment follow-up were clarified, and the IND number was added to the Title page.
17 October 2012	Prohibited medications and clarifications from protocol clarification letters were added. The statistical analysis sections was clarified, minor grammatical changes were made, and the inclusion and exclusion criteria were renumbered and expanded.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported