Clinical trial results:
Phase I/II Study of the Pharmacokinetics, Safety and Tolerability of Doravirine (MK-1439) and Doravirine/Lamivudine/Tenofovir Disoproxil Fumarate (MK-1439A) in HIV-1-infected Children and Adolescents

Summary

EudraCT number	2017-001518-27
Trial protocol	Outside EU/EEA
Global end of trial date	25 May 2022

Results information

Result version number	v1 (current)
This version publication date	15 December 2022
First version publication date	15 December 2022

Trial information

Trial identification

Sponsor protocol code	MK-1439-027

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03332095
WHO universal trial number (UTN)	-
Other trial identifiers	DAIDS-ES Registry Number: 34150, Other: IMPAACT 2014

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme LLC
Sponsor organisation address	126 East Lincoln Avenue, P.O. Box 2000, Rahway, NJ, United States, 07065
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001676-PIP01-14, EMEA-001695-PIP01-14
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 May 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 August 2020
Global end of trial reached?	Yes
Global end of trial date	25 May 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate the pharmacokinetics, safety, and tolerability of doravirine (also called MK-1439 or DOR) and doravirine/lamivudine/tenofovir disoproxil fumarate (also called MK-1439A or DOR/3TC/TDF) in human immunodeficiency virus (HIV)-1-infected children and adolescents.

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:

Participants in Cohort 1 received a combination of dolutegravir (DTG) or raltegravir (RAL) plus two nucleoside reverse transcriptase inhibitors (NRTIs). The Antiretroviral (ARV) medications were prescribed by participants' own health care providers and were not provided by the study.

Evidence for comparator: -

Actual start date of recruitment	02 July 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	South Africa: 9
Country: Number of subjects enrolled	Thailand: 35
Country: Number of subjects enrolled	United States: 11
Worldwide total number of subjects	55
EEA total number of subjects	0

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)	55

Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled from July 2018 to February 2020. Participants were recruited from 8 medical clinics in the United States, Thailand and South Africa.

Pre-assignment

Screening details:

There was no randomization. Enrollment started with Cohort 1, then Cohort 2 was open.

Period 1

Period 1 title	Enrolled
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: DOR

Arm description:

Participants received a single dose of DOR at study entry (Day 0).

Arm type	Experimental
Investigational medicinal product name	Doravirine (DOR)
Investigational medicinal product code	
Other name	MK-1439
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg of DOR administered orally

Arm title	Cohort 2: DOR/3TC/TDF

Arm description:

Participants received DOR/3TC/TDF from Day 0 through Week 96.

Arm type	Experimental
Investigational medicinal product name	Doravirine/Lamivudine/Tenofovir Disoproxil Fumarate (DOR/3TC/TDF)
Investigational medicinal product code	
Other name	MK-1439A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

DOR/3TC/TDF administered orally as a fixed-dose combination (as a tablet, 100 mg/300 mg/300 mg) once daily

Number of subjects in period 1	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF
Started	10	45
Received study treatment	9	45
Completed	9	45
Not completed	1	0
Enrolled but not treated	1	-

Period 2	
Period 2 title	Treated
Is this the baseline period?	Yes[1]
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	Yes
Arm title	Cohort 1: DOR

Arm description:

Participants received a single dose of DOR at study entry (Day 0).

Arm type	Experimental
Investigational medicinal product name	Doravirine (DOR)
Investigational medicinal product code	
Other name	MK-1439
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg of DOR administered orally

Arm title	Cohort 2: DOR/3TC/TDF

Arm description:

Participants received DOR/3TC/TDF from Day 0 through Week 96.

Arm type	Experimental
Investigational medicinal product name	Doravirine/Lamivudine/Tenofovir Disoproxil Fumarate (DOR/3TC/TDF)
Investigational medicinal product code	
Other name	MK-1439A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

DOR/3TC/TDF administered orally as a fixed-dose combination (as a tablet, 100 mg/300 mg/300 mg) once daily

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: The All Patients as Treated population was used as the baseline population.

Number of subjects in period 2[2]	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF
Started	9	45
Completed	9	42
Not completed	0	3
Pregnancy	-	2
Non-compliance with study drug	-	1

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The All Patients as Treated population was used as the baseline population.

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1: DOR
Reporting group description:	
Participants received a single dose of DOR at study entry (Day 0).	
Reporting group title	Cohort 2: DOR/3TC/TDF
Reporting group description:	
Participants received DOR/3TC/TDF from Day 0 through Week 96.	

Reporting group values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF	Total
Number of subjects	9	45	54
Age Categorical Units: Participants			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	9	45	54
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	14.3	15.0	
standard deviation	± 1.6	± 1.6	-
Gender Categorical Units: Participants			
Female	2	26	28
Male	7	19	26
Race Units: Subjects			
Black or African American	7	10	17
White	2	0	2
Asian	0	35	35
Ethnicity Units: Subjects			
Hispanic or Latino	0	1	1
Not Hispanic or Latino	9	44	53
Baseline Plasma HIV-1 RNA (copies/mL) Units: Subjects			
0 - <40	9	43	52
40 - <500,000	0	0	0
500,000 - <1,000,000	0	2	2
Weight Band (kg) Units: Subjects			

35 - <45 kg	1	0	1
≥ 45 kg	8	45	53
Region			
Units: Subjects			
Africa	0	9	9
Asia/Pacific	0	35	35
North America	9	1	10
Class of Prior ARTs			
Units: Subjects			
Nucleoside Reverse Transcriptase Inhibitors (NRTI)			
Non-Nucleoside Reverse Transcriptase Inhibitors			
Integrase Strand Transfer Inhibitors (INSTI)			
Protease Inhibitors (PI)			
Not Applicable			
Overall number of baseline subjects	9	45	54
CD4 Cell Count			
Units: Cells/mm^3			
arithmetic mean	788.2	717.8	
standard deviation	± 203.9	± 283.1	-
CD4 Percent			
Units: Percent			
arithmetic mean	36.2	33.1	
standard deviation	± 5.4	± 9.1	-
HIV-1 log10 RNA			
Units: Log10 copies/mL			
arithmetic mean	1.6	1.8	
standard deviation	± 0.0	± 0.9	-
Weight			
Units: kg			
arithmetic mean	55.9	53.8	
standard deviation	± 15.8	± 8.0	-
Duration of Prior ARTs			
Units: Days			
arithmetic mean	614.2	1882.3	
standard deviation	± 511.3	± 1649.6	-

Subject analysis sets

Subject analysis set title	Cohort 1: DOR
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received a single dose of DOR at study entry (Day 0).	
Subject analysis set title	Cohort 2: DOR/3TC/TDF
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received DOR/3TC/TDF from Day 0 through Week 96.	

Reporting group values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF	
Number of subjects	9	45	
Age Categorical Units: Participants			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: years arithmetic mean standard deviation	±	±	
Gender Categorical Units: Participants			
Female Male			
Race Units: Subjects			
Black or African American White Asian			
Ethnicity Units: Subjects			
Hispanic or Latino Not Hispanic or Latino			
Baseline Plasma HIV-1 RNA (copies/mL) Units: Subjects			
0 - <40 40 - <500,000 500,000 - <1,000,000			
Weight Band (kg) Units: Subjects			
35 - <45 kg ≥ 45 kg			
Region Units: Subjects			
Africa Asia/Pacific North America			
Class of Prior ARTs Units: Subjects			
Nucleoside Reverse Transcriptase Inhibitors (NRTI) Non-Nucleoside Reverse Transcriptase Inhibitors	9 0	43 32	

Integrase Strand Transfer Inhibitors (INSTI)	9	1	
Protease Inhibitors (PI)	0	10	
Not Applicable	0	2	
Overall number of baseline subjects	9	45	
CD4 Cell Count			
Units: Cells/mm^3			
arithmetic mean			
standard deviation	±	±	
CD4 Percent			
Units: Percent			
arithmetic mean			
standard deviation	±	±	
HIV-1 log10 RNA			
Units: Log10 copies/mL			
arithmetic mean			
standard deviation	±	±	
Weight			
Units: kg			
arithmetic mean			
standard deviation	±	±	
Duration of Prior ARTs			
Units: Days			
arithmetic mean			
standard deviation	±	±	

End points

End points reporting groups

Reporting group title	Cohort 1: DOR
Reporting group description:	
Participants received a single dose of DOR at study entry (Day 0).	
Reporting group title	Cohort 2: DOR/3TC/TDF
Reporting group description:	
Participants received DOR/3TC/TDF from Day 0 through Week 96.	
Reporting group title	Cohort 1: DOR
Reporting group description:	
Participants received a single dose of DOR at study entry (Day 0).	
Reporting group title	Cohort 2: DOR/3TC/TDF
Reporting group description:	
Participants received DOR/3TC/TDF from Day 0 through Week 96.	
Subject analysis set title	Cohort 1: DOR
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received a single dose of DOR at study entry (Day 0).	
Subject analysis set title	Cohort 2: DOR/3TC/TDF
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received DOR/3TC/TDF from Day 0 through Week 96.	

Primary: Pharmacokinetic (PK) Parameter: Single-dose Area-under-the-curve (AUC0-∞) of Doravirine (DOR) (Cohort 1)

End point title	Pharmacokinetic (PK) Parameter: Single-dose Area-under-the-curve (AUC0-∞) of Doravirine (DOR) (Cohort 1)[1]
End point description:	
Pharmacokinetic parameters were determined from plasma concentration-time profiles using non-compartmental methods (WinNonlin version 6.3, Pharsight Corp., Mountain View, CA). Area under the curve (AUC) was determined using non-compartmental analyses and estimated by the linear up/log down trapezoidal rule, from time zero to infinity. Steady state AUC0-24 is equivalent to single dose AUC0-∞. Cohort 1 participants who received the study treatment were analyzed.	
End point type	Primary
End point timeframe:	
Measured during the entry (day 0) visit. Blood samples were drawn at pre-dose, and at 1, 2, 4, 8, 12, 24, 48 and 72 hours post-dose.	
Notes:	
[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: No statistical analyses were planned for this endpoint.	

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	0[2]		
Units: µM*hr				
geometric mean (geometric coefficient of variation)	34.8 (± 43.2)	()		

Notes:

[2] - Cohort 2 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Primary: PK Parameter: Single-dose Maximum Concentration (Cmax) of DOR (Cohort 1)

End point title	PK Parameter: Single-dose Maximum Concentration (Cmax) of DOR (Cohort 1)[3]

End point description:

Pharmacokinetic parameters were determined from plasma concentration-time profiles using non-compartmental methods (WinNonlin, version 6.3, Pharsight Corp., Mountain View, CA). Cohort 1 participants who received the study treatment were analyzed.

End point type	Primary

End point timeframe:

Measured during the entry (day 0) visit. Blood samples were drawn at pre-dose, and at 1, 2, 4, 8, 12, 24, 48 and 72 hours post-dose.

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	0[4]		
Units: µM				
geometric mean (geometric coefficient of variation)	2.14 (± 25.9)	()		

Notes:

[4] - Cohort 2 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Primary: PK Parameter: Single-dose 24 Hour-concentration (C24hr) of DOR (Cohort 1)

End point title	PK Parameter: Single-dose 24 Hour-concentration (C24hr) of DOR (Cohort 1)[5]

End point description:

Pharmacokinetic parameters were determined from plasma concentration-time profiles using non-compartmental methods (WinNonlin, version 6.3, Pharsight Corp., Mountain View, CA). Cohort 1 participants who received the study treatment were analyzed.

End point type	Primary

End point timeframe:

Measured during the entry (day 0) visit. Blood samples were drawn at 24 hours post-dose.

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: No statistical analyses were planned for this endpoint.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	0[6]		
Units: nM				
geometric mean (geometric coefficient of variation)	514 (± 56.5)	()		

Notes:

[6] - Cohort 2 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Grade 3 or Higher Adverse Events (AEs) Assessed as Related to Study Drug

End point title	Percentage of Participants With Grade 3 or Higher Adverse Events (AEs) Assessed as Related to Study Drug[7]

End point description:

Percentage and Clopper-Pearson 95% Confidence Interval (CI) of participants with Grade 3 or higher AEs judged by the medical clinic as related to the study drug. AEs were graded based on the Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events (DAIDS AE Grading Table), Corrected Version 2.1, dated July 2017. Study participants who received at least one dose of study treatment were analyzed.

End point type	Primary

End point timeframe:

Cohort 1: Measured from Day 0 through Week 2; Cohort 2: Measured from Day 0 through Week 24.

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	45		
Units: Percentage of Participants				
number (confidence interval 95%)	0 (0.0 to 33.6)	0 (0.0 to 7.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Serious Adverse Events (SAEs) Assessed as Related to Study Drug

End point title	Percentage of Participants With Serious Adverse Events (SAEs) Assessed as Related to Study Drug[8]

End point description:

Percentage and Clopper-Pearson 95% CI of participants with SAEs judged by the medical clinic as related to the study drug. SAEs were reported according to Version 2.0 of the Manual for Expedited Reporting of Adverse Events to DAIDS (DAIDS EAE Manual). Study participants who received at least one dose of study treatment were analyzed.

End point type	Primary

End point timeframe:

Cohort 1: Measured from Day 0 through Week 2; Cohort 2: Measured from Day 0 through Week 24.

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	45		
Units: Percentage of Participants				
number (confidence interval 95%)	0 (0.0 to 33.6)	0 (0.0 to 7.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Permanent Discontinuation of Study Drug Due to Adverse Events Assessed as Related to Study Drug

End point title	Percentage of Participants With Permanent Discontinuation of Study Drug Due to Adverse Events Assessed as Related to Study Drug[9]

End point description:

Percentage and Clopper-Pearson 95% CI of participants with permanent discontinuation of study drug due to AEs judged by the medical clinic as related to the study drug. Study participants who received at least one dose of study treatment were analyzed.

End point type	Primary

End point timeframe:

Cohort 1: Measured from Day 0 through Week 2; Cohort 2: Measured from Day 0 through Week 24.

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	45		
Units: Percentage of Participants				
number (confidence interval 95%)	0 (0.0 to 33.6)	0 (0.0 to 7.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Grade 5 Adverse Events (Death) Regardless of Relationship to Study Drug

End point title	Percentage of Participants With Grade 5 Adverse Events (Death) Regardless of Relationship to Study Drug[10]

End point description:

Percentage and Clopper-Pearson 95% CI of participants with Grade 5 AEs (death) regardless of relationship to study drug. Study participants who received at least one dose of study treatment were analyzed.

End point type	Primary

End point timeframe:

Cohort 1: Measured from Day 0 through Week 2; Cohort 2: Measured from Day 0 through Week 24.

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	45		
Units: Percentage of Participants				
number (confidence interval 95%)	0 (0.0 to 33.6)	0 (0.0 to 7.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: AUC0-24hr of DOR (Cohort 2)

End point title	PK Parameter: AUC0-24hr of DOR (Cohort 2)

End point description:

Pharmacokinetic parameters were determined from plasma concentration-time profiles using non-compartmental methods (WinNonlin, version 6.3, Pharsight Corp., Mountain View, CA). Area under the curve (AUC) was determined using non-compartmental analyses and estimated by the linear up/log down trapezoidal rule, from time zero to 24 hours. Intensive PK samples were collected for the first ten participants enrolled in Cohort 2. The first 10 participants enrolled in Cohort 2 were analyzed.

End point type	Secondary

End point timeframe:

Measured at Week 1 visit. Blood samples were drawn at pre-dose, and at 2, 4, 12 and 24 hours post-dose.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[11]	10		
Units: µM*hr				
geometric mean (geometric coefficient of variation)	()	22.9 (± 47.0)		

Notes:

[11] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: AUC0-24hr of 3TC (Cohort 2)

End point title	PK Parameter: AUC0-24hr of 3TC (Cohort 2)

End point description:

Pharmacokinetic parameters were determined from plasma concentration-time profiles using non-compartmental methods (WinNonlin, version 6.3, Pharsight Corp., Mountain View, CA). Area under the curve (AUC) was determined using non-compartmental analyses and estimated by the linear up/log down trapezoidal rule, from time zero to 24 hours. Intensive PK samples were collected for the first ten participants enrolled in Cohort 2. The first 10 participants enrolled in Cohort 2 were analyzed.

End point type	Secondary

End point timeframe:

Measured at Week 1 visit. Blood samples were drawn at pre-dose, and at 1, 2, 4, 8, 12 and 24 hours post-dose.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[12]	10		
Units: h.ng/mL				
geometric mean (geometric coefficient of variation)	()	11300 (± 27.9)		

Notes:

[12] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: AUC0-24hr of Tenofovir (Cohort 2)

End point title	PK Parameter: AUC0-24hr of Tenofovir (Cohort 2)

End point description:

Pharmacokinetic parameters were determined from plasma concentration-time profiles using non-compartmental methods (WinNonlin, version 6.3, Pharsight Corp., Mountain View, CA). Area under the curve (AUC) was determined using non-compartmental analyses and estimated by the linear up/log down trapezoidal rule, from time zero to 24 hours. Intensive PK samples were collected for the first ten participants enrolled in Cohort 2. The first 10 participants enrolled in Cohort 2 were analyzed.

End point type	Secondary

End point timeframe:

Measured at Week 1 visit. Blood samples were drawn at pre-dose, and at 1, 2, 4, 8, 12 and 24 hours post-dose.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[13]	10		
Units: h.ng/mL				
geometric mean (geometric coefficient of variation)	()	2550 (± 14.3)		

Notes:

[13] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Cmax of DOR (Cohort 2)

End point title	PK Parameter: Cmax of DOR (Cohort 2)

End point description:

Pharmacokinetic parameters were determined from plasma concentration-time profiles using non-compartmental methods (WinNonlin, version 6.3, Pharsight Corp., Mountain View, CA). Cmax was projected from individual plasma concentration-time profiles using the non-parametric superposition function in WinNonLin v6.3. Intensive PK samples were collected for the first ten participants enrolled in Cohort 2. The first 10 participants enrolled in Cohort 2 were analyzed.

End point type	Secondary

End point timeframe:

Measured at Week 1 visit. Blood samples were drawn at pre-dose, and at 2, 4, 12 and 24 hours post-dose.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[14]	10		
Units: µM				
geometric mean (geometric coefficient of variation)	()	2.13 (± 42.7)		

Notes:

[14] - Cohort 1 was not analyzed for this endpoint

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Cmax of 3TC (Cohort 2)

End point title	PK Parameter: Cmax of 3TC (Cohort 2)

End point description:

Pharmacokinetic parameters were determined from plasma concentration-time profiles using non-compartmental methods (WinNonlin, version 6.3, Pharsight Corp., Mountain View, CA). Cmax was projected from individual plasma concentration-time profiles using the non-parametric superposition function in WinNonLin v6.3. Intensive PK samples were collected for the first ten participants enrolled in Cohort 2. The first 10 participants enrolled in Cohort 2 were analyzed.

End point type	Secondary

End point timeframe:

Measured at Week 1 visit. Blood samples were drawn at pre-dose, and at 1, 2, 4, 8, 12 and 24 hours post-dose.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[15]	10		
Units: ng/mL				
geometric mean (geometric coefficient of variation)	()	2100 (± 23.6)		

Notes:

[15] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Cmax of Tenofovir (Cohort 2)

End point title	PK Parameter: Cmax of Tenofovir (Cohort 2)

End point description:

Pharmacokinetic parameters were determined from plasma concentration-time profiles using non-compartmental methods (WinNonlin, version 6.3, Pharsight Corp., Mountain View, CA). Cmax was projected from individual plasma concentration-time profiles using the non-parametric superposition function in WinNonLin v6.3. Intensive PK samples were collected for the first ten participants enrolled in Cohort 2. The first 10 participants enrolled in Cohort 2 were analyzed.

End point type	Secondary

End point timeframe:

Measured at Week 1 visit. Blood samples were drawn at pre-dose, and at 1, 2, 4, 8, 12 and 24 hours post-dose.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[16]	10		
Units: ng/mL				
geometric mean (geometric coefficient of variation)	()	293 (± 36.6)		

Notes:

[16] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: C24hr of DOR (Cohort 2)

End point title	PK Parameter: C24hr of DOR (Cohort 2)

End point description:

Pharmacokinetic parameters were determined from plasma concentration-time profiles using non-compartmental methods (WinNonlin, version 6.3, Pharsight Corp., Mountain View, CA). C24hr was projected from individual plasma concentration-time profiles using the non-parametric superposition function in WinNonLin v6.3. Intensive PK samples were collected for the first ten participants enrolled in

Cohort 2. The first 10 participants enrolled in Cohort 2 were analyzed.

End point type	Secondary

End point timeframe:

Measured at Week 1 visit. Blood samples were drawn at 24 hours post-dose.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[17]	10		
Units: nM				
geometric mean (geometric coefficient of variation)	()	282 (± 73.8)		

Notes:

[17] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: C24hr of 3TC (Cohort 2)

End point title	PK Parameter: C24hr of 3TC (Cohort 2)

End point description:

Pharmacokinetic parameters were determined from plasma concentration-time profiles using non-compartmental methods (WinNonlin, version 6.3, Pharsight Corp., Mountain View, CA). C24hr was projected from individual plasma concentration-time profiles using the non-parametric superposition function in WinNonLin v6.3. Intensive PK samples were collected for the first ten participants enrolled in Cohort 2. The first 10 participants enrolled in Cohort 2 were analyzed.

End point type	Secondary

End point timeframe:

Measured at Week 1 visit. Blood samples were drawn at 24 hours post-dose.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[18]	10		
Units: ng/mL				
geometric mean (geometric coefficient of variation)	()	66.3 (± 54.7)		

Notes:

[18] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: C24hr of Tenofovir (Cohort 2)

End point title	PK Parameter: C24hr of Tenofovir (Cohort 2)

End point description:

Pharmacokinetic parameters were determined from plasma concentration-time profiles using non-compartmental methods (WinNonlin, version 6.3, Pharsight Corp., Mountain View, CA). C24hr was projected from individual plasma concentration-time profiles using the non-parametric superposition function in WinNonLin v6.3. Intensive PK samples were collected for the first ten participants enrolled in Cohort 2. The first 10 participants enrolled in Cohort 2 were analyzed.

End point type	Secondary

End point timeframe:

Measured at Week 1 visit. Blood samples were drawn at 24 hours post-dose.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[19]	10		
Units: ng/mL				
geometric mean (geometric coefficient of variation)	()	50.2 (± 9.4)		

Notes:

[19] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Plasma HIV-1 RNA Less Than 200 Copies/mL at Week 24 (Cohort 2)

End point title	Percentage of Participants With Plasma HIV-1 RNA Less Than 200 Copies/mL at Week 24 (Cohort 2)

End point description:

Virologic responses were assessed at week 24 as percentage (%) of participants and Clopper-Pearson 95% CI. Missing values were considered as failures for participants with missing data due to discontinuation of study drug as a result of virologic failure or for non-treatment related reasons with last available RNA >200 copies/mL; otherwise participants with missing values were excluded. Cohort 2 participants who received at least one dose of study treatment were analyzed. Participants who discontinued study for reasons other than virologic failure were excluded.

End point type	Secondary

End point timeframe:

Measured at week 24.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[20]	44		
Units: Percentage of Participants				
number (confidence interval 95%)	(to)	97.7 (88.0 to 99.9)		

Notes:

[20] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Plasma HIV-1 RNA Less Than 200 Copies/mL at Week 48 (Cohort 2)

End point title	Percentage of Participants With Plasma HIV-1 RNA Less Than 200 Copies/mL at Week 48 (Cohort 2)

End point description:

Virologic responses were assessed at week 48 as percentage (%) of participants and Clopper-Pearson 95% CI. Missing values were considered as failures for participants with missing data due to discontinuation of study drug as a result of virologic failure or for non-treatment related reasons with last available RNA >200 copies/mL; otherwise participants with missing values were excluded. Cohort 2 participants who received at least one dose of study treatment were analyzed. Participants who discontinued study for reasons other than virologic failure were excluded.

End point type	Secondary

End point timeframe:

Measured at week 48.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[21]	44		
Units: Percentage of Participants				
number (confidence interval 95%)	(to)	97.7 (88.0 to 99.9)		

Notes:

[21] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Plasma HIV-1 RNA Less Than 200 Copies/mL at Week 96 (Cohort 2)

End point title	Percentage of Participants With Plasma HIV-1 RNA Less Than 200 Copies/mL at Week 96 (Cohort 2)

End point description:

Virologic responses were assessed at week 96 as percentage (%) of participants and Clopper-Pearson 95% CI. Missing values were considered as failures for participants with missing data due to discontinuation of study drug as a result of virologic failure or for non-treatment related reasons with last available RNA >200 copies/mL; otherwise participants with missing values were excluded. Cohort 2 participants who received at least one dose of study treatment were analyzed. Participants who discontinued study for reasons other than virologic failure were excluded.

End point type	Secondary

End point timeframe:

Measured at week 96.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[22]	42		
Units: Percentage of Participants				
number (confidence interval 95%)	(to)	92.9 (80.5 to 98.5)		

Notes:

[22] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Plasma HIV-1 RNA Less Than 50 Copies/mL at Week 24 (Cohort 2)

End point title	Percentage of Participants With Plasma HIV-1 RNA Less Than 50 Copies/mL at Week 24 (Cohort 2)

End point description:

Virologic responses were assessed at week 24 as percentage of participants and Clopper-Pearson 95% CI. Missing values were considered as failures for participants with missing data due to discontinuation of study drug as a result of virologic failure or for non-treatment related reasons with last available RNA >50 copies/mL. Otherwise participants with missing values were excluded. Cohort 2 participants who received at least one dose of study treatment were analyzed. Participants who discontinued study for reasons other than virologic failure were excluded. One participant whose sample was diluted due to low volume, resulting in increased assay limit of quantification from 40 to 200 copies/mL was excluded.

End point type	Secondary

End point timeframe:

Measured at week 24.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[23]	43		
Units: Percentage of Participants				
number (confidence interval 95%)	(to)	97.7 (87.7 to 99.9)		

Notes:

[23] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Plasma HIV-1 RNA Less Than 50 Copies/mL at Week 48 (Cohort 2)

End point title	Percentage of Participants With Plasma HIV-1 RNA Less Than 50 Copies/mL at Week 48 (Cohort 2)

End point description:

Virologic responses were assessed at week 48 as percentage of participants and Clopper-Pearson 95% CI. Missing values were considered as failures for participants with missing data due to discontinuation of study drug as a result of virologic failure or for non-treatment related reasons with last available RNA >50 copies/mL. Otherwise participants with missing values were excluded. Cohort 2 participants who

received at least one dose of study treatment were analyzed. Participants who discontinued study for reasons other than virologic failure were excluded. Two participants whose samples were diluted due to low volume, resulting in increased assay limit of quantification from 40 to 200 copies/mL were excluded.

End point type	Secondary

End point timeframe:

Measured at week 48.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[24]	42		
Units: Percentage of Participants				
number (confidence interval 95%)	(to)	97.6 (87.4 to 99.9)		

Notes:

[24] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Plasma HIV-1 RNA Less Than 50 Copies/mL at Week 96 (Cohort 2)

End point title	Percentage of Participants With Plasma HIV-1 RNA Less Than 50 Copies/mL at Week 96 (Cohort 2)

End point description:

Virologic responses were assessed at week 96 as percentage of participants and Clopper-Pearson 95% CI. Missing values were considered as failures for participants with missing data due to discontinuation of study drug as a result of virologic failure or for non-treatment related reasons with last available RNA >50 copies/mL. Otherwise participants with missing values were excluded. Cohort 2 participants who received at least one dose of study treatment were analyzed. Participants who discontinued study for reasons other than virologic failure were excluded. Two participants whose samples were diluted due to low volume, resulting in increased assay limit of quantification from 40 to 200 copies/mL were excluded.

End point type	Secondary

End point timeframe:

Measured at week 96.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[25]	40		
Units: Percentage of Participants				
number (confidence interval 95%)	(to)	92.5 (79.6 to 98.4)		

Notes:

[25] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Plasma HIV-1 RNA Less Than 40 Copies/mL at Week 24 (Cohort 2)

End point title	Percentage of Participants With Plasma HIV-1 RNA Less Than 40 Copies/mL at Week 24 (Cohort 2)

End point description:

Virologic responses were assessed at week 24 as percentage (%) of participants and Clopper-Pearson 95% CI. Missing values were considered as failures for participants with missing data due to discontinuation of study drug as a result of virologic failure or for non-treatment related reasons with last available RNA >40 copies/mL; Otherwise participants with missing values were excluded. Cohort 2 participants who received at least one dose of study treatment were analyzed. Participants who discontinued study for reasons other than virologic failure were excluded. One participant whose sample was diluted due to low volume, resulting in increased assay limit of quantification from 40 to 200 copies/mL was excluded.

End point type	Secondary

End point timeframe:

Measured at week 24.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[26]	43		
Units: Percentage of Participants				
number (confidence interval 95%)	(to)	97.7 (87.7 to 99.9)		

Notes:

[26] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Plasma HIV-1 RNA Less Than 40 Copies/mL at Week 48 (Cohort 2)

End point title	Percentage of Participants With Plasma HIV-1 RNA Less Than 40 Copies/mL at Week 48 (Cohort 2)

End point description:

Virologic responses were assessed at week 48 as percentage (%) of participants and Clopper-Pearson 95% CI. Missing values were considered as failures for participants with missing data due to discontinuation of study drug as a result of virologic failure or for non-treatment related reasons with last available RNA >40 copies/mL; Otherwise participants with missing values were excluded. Cohort 2 participants who received at least one dose of study treatment were analyzed. Participants who discontinued study for reasons other than virologic failure were excluded. Two participants whose samples were diluted due to low volume, resulting in increased assay limit of quantification from 40 to 200 copies/mL were excluded.

End point type	Secondary

End point timeframe:

Measured at week 48.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[27]	42		
Units: Percentage of Participants				
number (confidence interval 95%)	(to)	97.6 (87.4 to 99.9)		

Notes:

[27] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Plasma HIV-1 RNA Less Than 40 Copies/mL at Week 96 (Cohort 2)

End point title	Percentage of Participants With Plasma HIV-1 RNA Less Than 40 Copies/mL at Week 96 (Cohort 2)

End point description:

Virologic responses were assessed at week 96 as percentage (%) of participants and Clopper-Pearson 95% CI. Missing values were considered as failures for participants with missing data due to discontinuation of study drug as a result of virologic failure or for non-treatment related reasons with last available RNA >40 copies/mL; Otherwise participants with missing values were excluded. Cohort 2 participants who received at least one dose of study treatment were analyzed. Participants who discontinued study for reasons other than virologic failure were excluded. Two participants whose samples were diluted due to low volume, resulting in increased assay limit of quantification from 40 to 200 copies/mL were excluded.

End point type	Secondary

End point timeframe:

Measured at week 96.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[28]	40		
Units: Percentage of Participants				
number (confidence interval 95%)	(to)	92.5 (79.6 to 98.4)		

Notes:

[28] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of log10 Drop From Baseline to Week 24 in Plasma HIV-1 RNA (ART-naive Participants) (Cohort 2)

End point title	Summary of log10 Drop From Baseline to Week 24 in Plasma HIV-1 RNA (ART-naive Participants) (Cohort 2)

End point description:

The differences between log10 HIV RNA at Week 24 minus at the Day 0 are summarized, and 95% CI calculated based on t-distribution, are presented. Cohort 2 participants who were ART-naive were analyzed.

End point type	Secondary

End point timeframe:

Measured at Day 0 and week 24.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[29]	2		
Units: Log10 plasma HIV-1 RNA				
arithmetic mean (confidence interval 95%)	(to)	-2.6 (-5.8 to 19.0)		

Notes:

[29] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of log10 Drop From Baseline to Week 48 in Plasma HIV-1 RNA (ART-naive Participants) (Cohort 2)

End point title	Summary of log10 Drop From Baseline to Week 48 in Plasma HIV-1 RNA (ART-naive Participants) (Cohort 2)

End point description:

The differences between log10 HIV RNA at Week 48 minus at the Day 0 are summarized, and 95% CI calculated based on t-distribution, are presented. Cohort 2 participants who were ART-naive were analyzed.

End point type	Secondary

End point timeframe:

Measured at Day 0 and week 48.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[30]	2		
Units: Log10 plasma HIV-1 RNA				
arithmetic mean (confidence interval 95%)	(to)	-2.1 (-5.8 to 26.1)		

Notes:

[30] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of log10 Drop From Baseline to Week 96 in Plasma HIV-1 RNA (ART-naive Participants) (Cohort 2)

End point title	Summary of log10 Drop From Baseline to Week 96 in Plasma HIV-1 RNA (ART-naive Participants) (Cohort 2)

End point description:

The differences between log10 HIV RNA at Week 96 minus at the Day 0 are summarized. Cohort 2 participants who were ART-naive and had Week 96 data available were analyzed. "9999" indicates dispersion could not be estimated due to low number of participants analyzed.

End point type	Secondary

End point timeframe:

Measured at Day 0 and week 96.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[31]	1		
Units: Log10 plasma HIV-1 RNA				
arithmetic mean (confidence interval 95%)	(to)	-4.3 (-9999 to 9999)		

Notes:

[31] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Changes in CD4 Count From Baseline to Week 24 (Cohort 2)

End point title	Summary of Changes in CD4 Count From Baseline to Week 24 (Cohort 2)

End point description:

The mean differences between CD4 count at Week 24 minus at the Day 0, and 95% CI calculated based on t-distribution, are presented. Cohort 2 participants who had non-missing values at both Day 0 and Week 24 timepoints were analyzed.

End point type	Secondary

End point timeframe:

Measured at Day 0 and week 24.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[32]	43		
Units: cells/mm^3				
arithmetic mean (confidence interval 95%)	(to)	84.8 (21.1 to 148.4)		

Notes:

[32] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Changes in CD4 Count From Baseline to Week 48 (Cohort 2)

End point title	Summary of Changes in CD4 Count From Baseline to Week 48 (Cohort 2)

End point description:

The mean differences between CD4 count at Week 48 minus at the Day 0, and 95% CI calculated based on t-distribution, are presented. Cohort 2 participants who had non-missing values at both Day 0 and Week 48 timepoints were analyzed.

End point type	Secondary

End point timeframe:

Measured at Day 0 and week 48.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[33]	43		
Units: cells/mm^3				
arithmetic mean (confidence interval 95%)	(to)	80.1 (14.2 to 146.0)		

Notes:

[33] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Changes in CD4 Count From Baseline to Week 96 (Cohort 2)

End point title	Summary of Changes in CD4 Count From Baseline to Week 96 (Cohort 2)

End point description:

The mean differences between CD4 count at Week 96 minus at the Day 0, and 95% CI calculated based on t-distribution, are presented. Cohort 2 participants who had non-missing values at both Day 0 and Week 96 timepoints were analyzed.

End point type	Secondary

End point timeframe:

Measured at Day 0 and week 96.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[34]	38		
Units: cells/mm^3				
arithmetic mean (confidence interval 95%)	(to)	42.5 (-31.1 to 116.1)		

Notes:

[34] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Changes in CD4 Percent From Baseline to Week 24 (Cohort 2)

End point title	Summary of Changes in CD4 Percent From Baseline to Week 24 (Cohort 2)

End point description:

The mean differences between CD4 percent at Week 24 minus at the Day 0, and 95% CI calculated based on t-distribution, are presented. Cohort 2 participants who had non-missing values at both Day 0 and Week 24 timepoints were analyzed.

End point type	Secondary

End point timeframe:

Measured at Day 0 and week 24.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[35]	43		
Units: Percent				
arithmetic mean (confidence interval 95%)	(to)	-1.5 (-2.8 to -0.2)		

Notes:

[35] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Changes in CD4 Percent From Baseline to Week 48 (Cohort 2)

End point title	Summary of Changes in CD4 Percent From Baseline to Week 48 (Cohort 2)

End point description:

The mean differences between CD4 percent at Week 48 minus at the Day 0, and 95% CI calculated based on t-distribution, are presented. Cohort 2 participants who had non-missing values at both Day 0 and Week 48 timepoints were analyzed.

End point type	Secondary

End point timeframe:

Measured at Day 0 and week 48.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[36]	43		
Units: Percent				
arithmetic mean (confidence interval 95%)	(to)	-0.4 (-1.7 to 0.9)		

Notes:

[36] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Changes in CD4 Percent From Baseline to Week 96 (Cohort 2)

End point title	Summary of Changes in CD4 Percent From Baseline to Week 96 (Cohort 2)

End point description:

The mean differences between CD4 percent at Week 96 minus at the Day 0, and 95% CI calculated based on t-distribution, are presented. Cohort 2 participants who had non-missing values at both Day 0 and Week 96 timepoints were analyzed.

End point type	Secondary

End point timeframe:

Measured at Day 0 and week 96.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[37]	38		
Units: Percent				
arithmetic mean (confidence interval 95%)	(to)	-0.5 (-2.5 to 1.5)		

Notes:

[37] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Grade 3 or Higher Adverse Events Assessed as Related to Study Drug (Cohort 2) Through End of Study

End point title	Percentage of Participants With Grade 3 or Higher Adverse Events Assessed as Related to Study Drug (Cohort 2) Through End of Study

End point description:

Percentage and Clopper-Pearson 95% CI of participants with Grade 3 or higher AEs judged by the medical clinic as related to the study drug. AEs were graded based on the Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events (DAIDS AE Grading Table), Corrected Version 2.1, dated July 2017 (DAIDS) AE Grading table corrected version 2.1. Cohort 2 participants who received at least one dose of study treatment were analyzed.

End point type	Secondary

End point timeframe:

Measured from Day 0 through Week 96.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[38]	45		
Units: Percentage of Participants				
number (confidence interval 95%)	(to)	0 (0.0 to 7.9)		

Notes:

[38] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Serious Adverse Events Assessed as Related to Study Drug (Cohort 2) Through End of Study

End point title	Percentage of Participants With Serious Adverse Events Assessed as Related to Study Drug (Cohort 2) Through End of Study

End point description:

Percentage and Clopper-Pearson 95% CI of participants with SAEs judged by the medical clinic as related to the study drug. SAEs were reported according to version 2.0 of the Manual for Expedited Reporting of Adverse Events to DAIDS (DAIDS EAE Manual). Cohort 2 participants who received at least one dose of study treatment were analyzed.

End point type	Secondary

End point timeframe:

Measured from Day 0 through Week 96.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[39]	45		
Units: Percentage of Participants				
number (confidence interval 95%)	(to)	0 (0.0 to 7.9)		

Notes:

[39] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Permanent Discontinuation of Study Drug Due to Adverse Events Assessed as Related to Study Drug (Cohort 2) Through End of Study

End point title	Percentage of Participants With Permanent Discontinuation of Study Drug Due to Adverse Events Assessed as Related to Study Drug (Cohort 2) Through End of Study

End point description:

Percentage and Clopper-Pearson 95% CI of participants with permanent discontinuation of study drug due to AEs judged by the medical clinic as related to the study drug. Cohort 2 participants who received at least one dose of study treatment were analyzed.

End point type	Secondary

End point timeframe:

Measured from Day 0 through Week 96.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[40]	45		
Units: Percentage of Participants				
number (confidence interval 95%)	(to)	0 (0.0 to 7.9)		

Notes:

[40] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Grade 5 Adverse Events (Death) Regardless of Relationship to Study Drug (Cohort 2) Through End of Study

End point title	Percentage of Participants With Grade 5 Adverse Events (Death) Regardless of Relationship to Study Drug (Cohort 2) Through End of Study

End point description:

Percentage and Clopper-Pearson 95% CI of participants with Grade 5 adverse events (death). Cohort 2 participants who received at least one dose of study treatment were analyzed.

End point type	Secondary

End point timeframe:

Measured from Day 0 through Week 96.

End point values	Cohort 1: DOR	Cohort 2: DOR/3TC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[41]	45		
Units: Percentage of Participants				
number (confidence interval 95%)	(to)	0 (0.0 to 7.9)		

Notes:

[41] - Cohort 1 was not analyzed for this end point.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of study treatment to study completion at Week 2 in Cohort 1 or at Week 96 in Cohort 2.

Adverse event reporting additional description:

All-cause mortality was summarized for all allocated participants and AEs were summarized for participants who received at least 1 dose of study drug. AE severity grading was based on the DAIDS AE Grading Table, Corrected Version 2.1. SAEs were graded using DAIDS EAE Manual V2.0.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Cohort 2: DOR/3TC/TDF

Reporting group description:

Participants received DOR/3TC/TDF from Day 0 through Week 96.

Reporting group title	Cohort 1: DOR

Reporting group description:

Participants received a single dose of DOR at study entry (Day 0).

Serious adverse events	Cohort 2: DOR/3TC/TDF	Cohort 1: DOR	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 45 (4.44%)	0 / 9 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 45 (2.22%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Lip injury			
subjects affected / exposed	1 / 45 (2.22%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			

subjects affected / exposed	1 / 45 (2.22%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis C			
subjects affected / exposed	1 / 45 (2.22%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scrotal abscess			
subjects affected / exposed	1 / 45 (2.22%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cohort 2: DOR/3TC/TDF	Cohort 1: DOR	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	45 / 45 (100.00%)	4 / 9 (44.44%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	21 / 45 (46.67%)	0 / 9 (0.00%)	
occurrences (all)	87	0	
Aspartate aminotransferase increased			
subjects affected / exposed	15 / 45 (33.33%)	2 / 9 (22.22%)	
occurrences (all)	38	2	
Blood albumin decreased			
subjects affected / exposed	3 / 45 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	3	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	14 / 45 (31.11%)	1 / 9 (11.11%)	
occurrences (all)	47	1	

Blood bicarbonate decreased			
subjects affected / exposed	12 / 45 (26.67%)	0 / 9 (0.00%)	
occurrences (all)	17	0	
Blood cholesterol increased			
subjects affected / exposed	6 / 45 (13.33%)	0 / 9 (0.00%)	
occurrences (all)	10	0	
Blood creatinine increased			
subjects affected / exposed	21 / 45 (46.67%)	0 / 9 (0.00%)	
occurrences (all)	73	0	
Blood glucose decreased			
subjects affected / exposed	6 / 45 (13.33%)	0 / 9 (0.00%)	
occurrences (all)	8	0	
Blood glucose increased			
subjects affected / exposed	8 / 45 (17.78%)	1 / 9 (11.11%)	
occurrences (all)	12	1	
Blood phosphorus decreased			
subjects affected / exposed	4 / 45 (8.89%)	0 / 9 (0.00%)	
occurrences (all)	5	0	
Blood phosphorus increased			
subjects affected / exposed	0 / 45 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Blood potassium decreased			
subjects affected / exposed	9 / 45 (20.00%)	0 / 9 (0.00%)	
occurrences (all)	20	0	
Blood pressure increased			
subjects affected / exposed	8 / 45 (17.78%)	0 / 9 (0.00%)	
occurrences (all)	31	0	
Blood sodium decreased			
subjects affected / exposed	7 / 45 (15.56%)	0 / 9 (0.00%)	
occurrences (all)	7	0	
Carbon dioxide decreased			
subjects affected / exposed	11 / 45 (24.44%)	0 / 9 (0.00%)	
occurrences (all)	59	0	
Blood triglycerides increased			
subjects affected / exposed	3 / 45 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	6	0	

Glomerular filtration rate decreased			
subjects affected / exposed	25 / 45 (55.56%)	0 / 9 (0.00%)	
occurrences (all)	117	0	
Haemoglobin decreased			
subjects affected / exposed	7 / 45 (15.56%)	0 / 9 (0.00%)	
occurrences (all)	13	0	
Lipase increased			
subjects affected / exposed	8 / 45 (17.78%)	0 / 9 (0.00%)	
occurrences (all)	26	0	
Neutrophil count decreased			
subjects affected / exposed	3 / 45 (6.67%)	1 / 9 (11.11%)	
occurrences (all)	3	1	
Injury, poisoning and procedural complications			
Adverse event following immunisation			
subjects affected / exposed	5 / 45 (11.11%)	0 / 9 (0.00%)	
occurrences (all)	6	0	
Nervous system disorders			
Headache			
subjects affected / exposed	9 / 45 (20.00%)	0 / 9 (0.00%)	
occurrences (all)	10	0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 45 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	3	0	
Eye disorders			
Conjunctival pallor			
subjects affected / exposed	3 / 45 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	3	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	6 / 45 (13.33%)	1 / 9 (11.11%)	
occurrences (all)	7	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	9 / 45 (20.00%)	0 / 9 (0.00%)	
occurrences (all)	11	0	

Nasal congestion			
subjects affected / exposed	6 / 45 (13.33%)	0 / 9 (0.00%)	
occurrences (all)	7	0	
Oropharyngeal pain			
subjects affected / exposed	5 / 45 (11.11%)	0 / 9 (0.00%)	
occurrences (all)	8	0	
Productive cough			
subjects affected / exposed	5 / 45 (11.11%)	0 / 9 (0.00%)	
occurrences (all)	5	0	
Rhinorrhoea			
subjects affected / exposed	8 / 45 (17.78%)	0 / 9 (0.00%)	
occurrences (all)	8	0	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	4 / 45 (8.89%)	0 / 9 (0.00%)	
occurrences (all)	4	0	
Papule			
subjects affected / exposed	3 / 45 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	4	0	
Pruritus			
subjects affected / exposed	4 / 45 (8.89%)	0 / 9 (0.00%)	
occurrences (all)	4	0	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	3 / 45 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	3	0	
Proteinuria			
subjects affected / exposed	6 / 45 (13.33%)	0 / 9 (0.00%)	
occurrences (all)	11	0	
Infections and infestations			
COVID-19			
subjects affected / exposed	3 / 45 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	3	0	
Nasopharyngitis			
subjects affected / exposed	4 / 45 (8.89%)	0 / 9 (0.00%)	
occurrences (all)	4	0	
Metabolism and nutrition disorders			

Hypertriglyceridaemia subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 4	0 / 9 (0.00%) 0	
Hypokalaemia subjects affected / exposed occurrences (all)	4 / 45 (8.89%) 5	0 / 9 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 June 2018	Amendment 01: Primary reason for amendment was to update testing and procedures.
10 June 2019	Amendment 02: Primary reason for amendment was to update target enrollment requirements and subject inclusion criterion.
01 July 2020	Amendment 03: Primary reason for amendment was to clarify procedural specifications.
03 September 2021	Amendment 04: Primary reason for amendment was to extend the allowable follow-up period for participants.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported