Clinical trial results:
A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study of the Safety and Efficacy of Tenofovir DF as Part of an Optimized Antiretroviral Regimen in HIV-1-Infected Adolescents

Summary

EudraCT number	2015-000727-85
Trial protocol	Outside EU/EEA
Global end of trial date	19 December 2013

Results information

Result version number	v1 (current)
This version publication date	22 March 2016
First version publication date	05 August 2015

Trial information

Trial identification

Sponsor protocol code	GS-US-104-0321

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00352053
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Clinical Trial Mailbox, Gilead Sciences International Ltd , ClinicalTrialDisclosures@gilead.com
Scientific contact	Clinical Trial Mailbox, Gilead Sciences International Ltd , ClinicalTrialDisclosures@gilead.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000533-PIP01-08
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	19 December 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 December 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to assess the safety and efficacy of tenofovir disoproxil fumarate (tenofovir DF; TDF) plus a genotype-guided optimized background regimen (OBR) compared to placebo plus OBR in the treatment of human immunodeficiency virus type 1 (HIV-1) infected antiretroviral treatment-experienced adolescents with plasma HIV-1 ribonucleic acid (RNA) levels greater than or equal to 1000 copies/mL.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy:

All participants received a genotype-guided optimized background regimen (OBR) consisting of a minimum of 3 and a maximum of 5 antiretroviral agents (ARV) for the duration of the study.

Evidence for comparator: -

Actual start date of recruitment	13 June 2006
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Brazil: 86
Country: Number of subjects enrolled	Panama: 4
Worldwide total number of subjects	90
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)	90
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

There were 17 sites in Brazil and 1 site in Panama. First participant was screened on 13 June 2006. The last study visit occurred on 19 December 2013.

Pre-assignment

Screening details:

123 participants were screened.

Period 1

Period 1 title	Randomized Phase (Through Week 48)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

Participants were randomized to either TDF or placebo, plus a genotype-guided optimized background regimen (OBR) consisting of 3 minimum (min.) to 5 maximum (max.) antiretroviral (ARV) agents.

Participants in the TDF group who experienced virologic failure (VF) during the randomized phase discontinued the study. Participants in the placebo group who experienced VF discontinued the randomized phase, and were eligible to enroll early in the first open-label TDF extension phase.

Arms

Are arms mutually exclusive?	Yes
Arm title	Tenofovir DF

Arm description:

TDF+OBR from baseline to Week 48 (double-blind phase), followed by open-label TDF+OBR for up to an additional 288 weeks.

Arm type	Experimental
Investigational medicinal product name	Tenofovir DF
Investigational medicinal product code	
Other name	Viread®, TDF
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tenofovir DF 300 mg tablet administered orally once daily

Arm title	Placebo

Arm description:

Placebo to match TDF+OBR from baseline to Week 48 (double-blind phase), followed by open-label TDF+OBR for up to an additional 288 weeks.

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

Dosage and administration details:

Placebo to match tenofovir DF 300 administered orally once daily

Number of subjects in period 1[1]	Tenofovir DF	Placebo
Started	45	42
Switched to open-label TDF after VF	0 [2]	10 [3]
Completed	27	36
Not completed	18	6
Physician decision	2	4
Virologic failure	14	-
Adverse event, non-fatal	1	-
Intolerance to Antiretroviral Regimen	1	-
Withdrawal by subject	-	2

Notes:

[1] - 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: 3 participants who were enrolled but not treated are not included in the subject disposition table.
[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: No participants randomized to TDF who discontinued the double-blind phase due to VF were enrolled in the 1st open-label extension phase.
[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: 10 participants randomized to placebo experienced VF, discontinued the double-blind phase, and enrolled early in the 1st open-label TDF extension phase.

Period 2

Period 2 title	First Extension Phase (Weeks 48-144)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Tenofovir DF

Arm description:

TDF+OBR from baseline to Week 48 (double-blind phase), followed by open-label TDF+OBR for up to an additional 288 weeks.

Arm type	Experimental
Investigational medicinal product name	Tenofovir DF
Investigational medicinal product code	
Other name	Viread®, TDF
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tenofovir DF 300 mg tablet administered orally once daily

Arm title	Placebo

Arm description:

Placebo to match TDF+OBR from baseline to Week 48 (double-blind phase), followed by open-label TDF+OBR for up to an additional 288 weeks.

Arm type	Experimental

Investigational medicinal product name	Tenofovir DF
Investigational medicinal product code	
Other name	Viread®, TDF
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tenofovir DF 300 mg tablet administered orally once daily

Number of subjects in period 2[4]	Tenofovir DF	Placebo
Started	24	36
Completed	12	19
Not completed	12	17
Physician decision	9	13
Pregnancy	1	-
Lost to follow-up	1	-
Lack of efficacy	1	4

Notes:

[4] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: 3 participants in the Tenofovir DF Group who completed the Randomized Phase did not continue in the First Extension Phase.

Period 3

Period 3 title	Second Extension Phase (Weeks 144-240)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Tenofovir DF

Arm description:

TDF+OBR from baseline to Week 48 (double-blind phase), followed by open-label TDF+OBR for up to an additional 288 weeks.

Arm type	Experimental
Investigational medicinal product name	Tenofovir DF
Investigational medicinal product code	
Other name	Viread®, TDF
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tenofovir DF 300 mg tablet administered orally once daily

Arm title	Placebo

Arm description:

Placebo to match TDF+OBR from baseline to Week 48 (double-blind phase), followed by open-label TDF+OBR for up to an additional 288 weeks.

Arm type	Experimental

Investigational medicinal product name	Tenofovir DF
Investigational medicinal product code	
Other name	Viread®, TDF
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tenofovir DF 300 mg tablet administered orally once daily

Number of subjects in period 3[5]	Tenofovir DF	Placebo
Started	9	14
Completed	4	9
Not completed	5	5
Physician decision	4	4
Withdrawal by subject	1	1

Notes:

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

Justification: 3 participants in the Tenofovir DF Group and 5 participants in the Placebo Group who completed the First Extension Phase did not continue in the Second Extension Phase.

Period 4

Period 4 title	Third Extension Phase (Weeks 240-294)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Tenofovir DF

Arm description:

TDF+OBR from baseline to Week 48 (double-blind phase), followed by open-label TDF+OBR for up to an additional 288 weeks.

Arm type	Experimental
Investigational medicinal product name	Tenofovir DF
Investigational medicinal product code	
Other name	Viread®, TDF
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tenofovir DF 300 mg tablet administered orally once daily

Arm title	Placebo

Arm description:

Placebo to match TDF+OBR from baseline to Week 48 (double-blind phase), followed by open-label TDF+OBR for up to an additional 288 weeks.

Arm type	Experimental

Investigational medicinal product name	Tenofovir DF
Investigational medicinal product code	
Other name	Viread®, TDF
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tenofovir DF 300 mg tablet administered orally once daily

Number of subjects in period 4[6]	Tenofovir DF	Placebo
Started	1	4
Completed	0	2
Not completed	1	2
Lack of efficacy	1	1
Withdrawal by subject	-	1

Notes:

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

Justification: 3 participants in the Tenofovir DF Group and 5 participants in the Placebo Group who completed the Second Extension Phase did not continue in the Third Extension Phase.

Baseline characteristics

Reporting groups	
Reporting group title	Tenofovir DF
Reporting group description:	
TDF+OBR from baseline to Week 48 (double-blind phase), followed by open-label TDF+OBR for up to an additional 288 weeks.	
Reporting group title	Placebo
Reporting group description:	
Placebo to match TDF+OBR from baseline to Week 48 (double-blind phase), followed by open-label TDF+OBR for up to an additional 288 weeks.	

Reporting group values	Tenofovir DF	Placebo	Total
Number of subjects	45	42	87
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	14	14	
standard deviation	± 1.5	± 1.5	-
Gender categorical Units: Subjects			
Female	24	25	49
Male	21	17	38
Ethnicity Units: Subjects			
Hispanic or Latino	45	42	87
Not Hispanic or Latino	0	0	0
Unknown or Not Reported	0	0	0
Race Units: Subjects			
White	23	22	45
Black or African Heritage	14	11	25
Mulatto	4	4	8
Mixed Race	1	2	3
Indian Descendant	1	1	2
Mestizo	0	2	2
Black and White Race	1	0	1
South American Indian	1	0	1
Body Mass Index Units: kg/m^2			
arithmetic mean	18.72	19.99	
standard deviation	± 2.304	± 3.238	-
CD4 Cell Count Units: cells/mm^3			
arithmetic mean	390	357	
standard deviation	± 244	± 200.8	-
CD4 Percentage			

CD4 percentage is the percentage of total lymphocytes that are CD4 cells.			
Units: Percentage of CD4 lymphocytes			
arithmetic mean	17.8	17.6	
standard deviation	± 9.7	± 8.31	-
Height			
Units: cm			
arithmetic mean	155.84	156.05	
standard deviation	± 10.071	± 8.569	-
Human Immunodeficiency virus type 1 (HIV-1) ribonucleic acid (RNA)			
Units: log10 copies/mL			
arithmetic mean	4.71	4.56	
standard deviation	± 0.723	± 0.746	-
Weight			
Units: kg			
arithmetic mean	45.84	49.09	
standard deviation	± 9.639	± 11.342	-

End points

End points reporting groups

Reporting group title	Tenofovir DF

Reporting group description:

TDF+OBR from baseline to Week 48 (double-blind phase), followed by open-label TDF+OBR for up to an additional 288 weeks.

Reporting group title	Placebo

Reporting group description:

Placebo to match TDF+OBR from baseline to Week 48 (double-blind phase), followed by open-label TDF+OBR for up to an additional 288 weeks.

Reporting group title	Tenofovir DF

Reporting group description:

TDF+OBR from baseline to Week 48 (double-blind phase), followed by open-label TDF+OBR for up to an additional 288 weeks.

Reporting group title	Placebo

Reporting group description:

Placebo to match TDF+OBR from baseline to Week 48 (double-blind phase), followed by open-label TDF+OBR for up to an additional 288 weeks.

Reporting group title	Tenofovir DF

Reporting group description:

TDF+OBR from baseline to Week 48 (double-blind phase), followed by open-label TDF+OBR for up to an additional 288 weeks.

Reporting group title	Placebo

Reporting group description:

Placebo to match TDF+OBR from baseline to Week 48 (double-blind phase), followed by open-label TDF+OBR for up to an additional 288 weeks.

Reporting group title	Tenofovir DF

Reporting group description:

TDF+OBR from baseline to Week 48 (double-blind phase), followed by open-label TDF+OBR for up to an additional 288 weeks.

Reporting group title	Placebo

Reporting group description:

Placebo to match TDF+OBR from baseline to Week 48 (double-blind phase), followed by open-label TDF+OBR for up to an additional 288 weeks.

Subject analysis set title	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants who were randomized to placebo and switched to open-label TDF 300 mg tablets (plus OBR) with HIV-1 RNA < 1000 copies/mL at the time of the switch when a new baseline was established. The analysis time point is calculated as the number of weeks after the switch.

Subject analysis set title	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants who were randomized to placebo and switched to open-label TDF 300 mg tablets (plus OBR) with HIV-1 RNA ≥ 1000 copies/mL at the time of the switch when a new baseline was established. The analysis time point is calculated as the number of weeks after the switch.

Primary: Time-weighted average change from baseline through Week 24 (DAVG24) in plasma HIV-1 RNA

End point title	Time-weighted average change from baseline through Week 24 (DAVG24) in plasma HIV-1 RNA

End point description:

DAVG24 was defined as the time-weighted average between the first postbaseline value through the last value up to Week 24 minus the baseline value. DAVG24 was calculated using the trapezoidal rule with

all available postbaseline data minus the baseline value.

Data for participants who discontinued the randomized (double-blind) phase of the study early were included up until the point of study discontinuation (missing data not imputed). For the TDF and Placebo groups, only data collected during the double-blind phase are included.

Intent-to-treat (ITT) Analysis Set: participants who were randomized and received at least 1 dose of study drug, with baseline HIV-1 RNA ≥ 1000 copies/mL and who had no major eligibility criteria violations.

End point type	Primary

End point timeframe:

Baseline to 24 Weeks

End point values	Tenofovir DF	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	41		
Units: log10 copies/mL				
median (inter-quartile range (Q1-Q3))	-1.58 (-2.15 to -0.27)	-1.549 (-2.36 to -0.34)		

Statistical analyses

Statistical analysis title	Difference in change from baseline

Statistical analysis description:

Null hypothesis: Time-weighted average changes from baseline through Week 24 in plasma HIV-1 RNA for the tenofovir DF and placebo groups are equal. Alternative hypothesis: Time-weighted average changes from baseline through Week 24 in plasma HIV-1 RNA for the tenofovir DF and placebo groups are different (two-sided).

Comparison groups	Tenofovir DF v Placebo
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.55 [2]
Method	Van Elteren test

Notes:

[1] - Intergroup analysis

[2] - No adjustments for multiple comparisons were made. P-value is from a Van Elteren test stratified by baseline genotypic sensitivity score (GSS) (without tenofovir DF) <= or > median (median GSS is 2).

Secondary: Time-weighted average change from baseline through Week 48 (DAVG48) in plasma HIV-1 RNA

End point title	Time-weighted average change from baseline through Week 48 (DAVG48) in plasma HIV-1 RNA

End point description:

DAVG48 was defined as the time-weighted average between the first postbaseline value through the last value up to Week 48 minus the baseline value. DAVG48 was calculated using the trapezoidal rule with all available postbaseline data minus the baseline value.

Data for participants who discontinued the double-blind phase of the study early were included up until the point of discontinuation from the study (ie, missing data were not imputed). For the TDF and Placebo groups, only data collected during the double-blind phase are included.

ITT Analysis Set

End point type	Secondary

End point timeframe:

Baseline to 48 weeks

End point values	Tenofovir DF	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	41		
Units: log10 copies/mL				
median (inter-quartile range (Q1-Q3))	-1.423 (-2.25 to -0.25)	-1.352 (-2.72 to -0.53)		

Statistical analyses

Statistical analysis title	Difference in change from baseline

Statistical analysis description:

Null hypothesis: Time-weighted average changes from baseline through Week 48 in plasma HIV-1 RNA for the tenofovir DF and placebo groups are equal. Alternative hypothesis: Time-weighted average changes from baseline through Week 48 in plasma HIV-1 RNA for the tenofovir DF and placebo groups are different (two-sided).

Comparison groups	Tenofovir DF v Placebo
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 0.4 [4]
Method	Van Elteren test

Notes:

[3] - Intergroup analysis

[4] - No adjustments for multiple comparisons were made. P-value is from a Van Elteren test stratified by baseline GSS (without tenofovir DF) <= or > median (median GSS is 2).

Secondary: Change from baseline to Week 24 in HIV-1 RNA

End point title	Change from baseline to Week 24 in HIV-1 RNA

End point description:

ITT Analysis Set. The Tenofovir DF and Placebo groups were analyzed using the last observation carried forward (LOCF) method (includes the participant's last available postbaseline value for missing data). The Placebo/TDF groups were analyzed using the missing = excluded method (participants with missing data were excluded from the analysis). For the TDF and Placebo groups, only data collected during the double-blind phase are included.

End point type	Secondary

End point timeframe:

Baseline to 24 weeks

End point values	Tenofovir DF	Placebo	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	44	41	18	16
Units: log10 copies/mL				
median (inter-quartile range (Q1-Q3))	-1.23 (-2.3 to -0.1)	-1.27 (-2.8 to -0.1)	0 (0 to 0)	-0.1 (-0.6 to 0.3)

Statistical analyses

Statistical analysis title	Difference in change from baseline

Statistical analysis description:

Null hypothesis: Changes from baseline through Week 24 in plasma HIV-1 RNA for the tenofovir DF and placebo groups are equal. Alternative hypothesis: Changes from baseline through Week 24 in plasma HIV-1 RNA for the tenofovir DF and placebo groups are different (two-sided).

Comparison groups	Tenofovir DF v Placebo
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	= 0.58 [6]
Method	Van Elteren test

Notes:

[5] - Intergroup analysis

[6] - No adjustments for multiple comparisons were made. P-value is from a Van Elteren test stratified by baseline GSS (without tenofovir DF) <= or > median (median GSS is 2).

Secondary: Change from baseline to Week 48 in HIV-1 RNA

End point title	Change from baseline to Week 48 in HIV-1 RNA

End point description:

ITT Analysis Set. The Tenofovir DF and Placebo groups were analyzed using the LOCF method. The Placebo/TDF groups were analyzed using the missing = excluded method. For the TDF and Placebo groups, only data collected during the double-blind phase are included.

End point type	Secondary

End point timeframe:

Baseline to 48 weeks

End point values	Tenofovir DF	Placebo	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	44	41	18	8
Units: log10 copies/mL				
median (inter-quartile range (Q1-Q3))	-0.97 (-2.3 to 0)	-1.53 (-3 to 0)	0 (0 to 0.6)	0.2 (-0.1 to 0.5)

Statistical analyses

Statistical analysis title	Difference in change from baseline

Statistical analysis description:

Null hypothesis: Changes from baseline through Week 48 in plasma HIV-1 RNA for the tenofovir DF and placebo groups are equal. Alternative hypothesis: Changes from baseline through Week 48 in plasma HIV-1 RNA for the tenofovir DF and placebo groups are different (two-sided).

Comparison groups	Placebo v Tenofovir DF
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	other[7]
P-value	= 0.37 [8]
Method	Van Elteren test

Notes:

[7] - Intergroup analysis

[8] - No adjustments for multiple comparisons were made. P-value is from a Van Elteren test stratified by baseline GSS (without tenofovir DF) <= or > median (median GSS is 2).

Secondary: Change from Baseline to Week 96 in HIV-1 RNA

End point title	Change from Baseline to Week 96 in HIV-1 RNA[9]

End point description:

ITT Analysis Set, missing = excluded method

End point type	Secondary

End point timeframe:

Baseline to 96 weeks

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	19	17	3	
Units: log10 copies/mL				
median (inter-quartile range (Q1-Q3))	-2.1 (-2.5 to -0.6)	0 (0 to 0.9)	0.1 (-1.4 to 0.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 144 in HIV-1 RNA

End point title	Change from baseline to Week 144 in HIV-1 RNA[10]

End point description:

ITT Analysis Set, missing = excluded method

End point type	Secondary

End point timeframe:

Baseline to 144 weeks

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	11	2	
Units: log10 copies/mL				
median (inter-quartile range (Q1-Q3))	-2.5 (-2.7 to -2.2)	0.2 (0 to 1.6)	0.7 (0.6 to 0.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Week 192 in HIV-1 RNA

End point title	Change From Baseline to Week 192 in HIV-1 RNA[11]

End point description:

ITT Analysis Set, missing = excluded method

End point type	Secondary

End point timeframe:

Baseline to 192 weeks

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	7	5	2	
Units: log10 copies/mL				
median (inter-quartile range (Q1-Q3))	-2 (-2.5 to -0.7)	0 (0 to 0.2)	-0.1 (-1.4 to 1.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 240 in HIV-1 RNA

End point title	Change from baseline to Week 240 in HIV-1 RNA[12]

End point description:

ITT Analysis Set, missing = excluded method

End point type	Secondary

End point timeframe:

Baseline to 240 weeks

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	2	1	
Units: log10 copies/mL				
median (inter-quartile range (Q1-Q3))	-2.5 (-2.6 to -2.2)	-0.4 (-0.8 to 0)	-1.4 (-1.4 to -1.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 288 in HIV-1 RNA

End point title	Change from Baseline to Week 288 in HIV-1 RNA[13]

End point description:

ITT Analysis Set, missing = excluded method

End point type	Secondary

End point timeframe:

Baseline to 288 weeks

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	1	1	1	
Units: log10 copies/mL				
median (inter-quartile range (Q1-Q3))	-1.1 (-1.1 to -1.1)	-0.8 (-0.8 to -0.8)	0.6 (0.6 to 0.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 336 in HIV-1 RNA

End point title	Change from baseline to Week 336 in HIV-1 RNA[14]

End point description:

ITT Analysis Set, missing = excluded method

No analysis was performed because the last study participant discontinued after Week 294 and the study was closed.

End point type	Secondary

End point timeframe:

Baseline to 336 weeks

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[15]	0[16]	0[17]	
Units: log10 copies/mL				
median (inter-quartile range (Q1-Q3))	(to)	(to)	(to)	

Notes:

[15] - No analysis was performed because the study ended early after Week 294.

[16] - No analysis was performed because the study ended early after Week 294.

[17] - No analysis was performed because the study ended early after Week 294.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 24 in Cluster Determinant 4 (CD4) count

End point title	Change from baseline to Week 24 in Cluster Determinant 4 (CD4) count

End point description:

ITT Analysis Set, missing = excluded method

For the TDF and Placebo groups, only data collected during the double-blind phase are included.

End point type	Secondary

End point timeframe:

Baseline to 24 weeks

End point values	Tenofovir DF	Placebo	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	42	41	18	16
Units: cells/mm3				
median (inter-quartile range (Q1-Q3))	69 (-26 to 172)	49 (-3 to 156)	-43 (-181 to 53)	-12 (-48 to 59)

Statistical analyses

Statistical analysis title	Difference in change from baseline

Statistical analysis description:

Null hypothesis: Changes from baseline through Week 24 in plasma CD4 count for the tenofovir DF and placebo groups are equal. Alternative hypothesis: Changes from baseline through Week 24 in CD4 count for the tenofovir DF and placebo groups are different (two-sided).

Comparison groups	Tenofovir DF v Placebo
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other[18]
P-value	= 0.71 [19]
Method	Van Elteren test

Notes:

[18] - Intergroup analysis

[19] - No adjustments for multiple comparisons were made. P-value is from a Van Elteren test stratified by baseline GSS (without tenofovir DF) <= or > median (median GSS is 2).

Secondary: Change from baseline to Week 48 in CD4 count

End point title	Change from baseline to Week 48 in CD4 count

End point description:

ITT Analysis Set, missing = excluded method

For the TDF and Placebo groups, only data collected during the double-blind phase are included.

End point type	Secondary

End point timeframe:

Baseline to 48 weeks

End point values	Tenofovir DF	Placebo	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	32	31	17	11
Units: cells/mm3				
median (inter-quartile range (Q1-Q3))	152 (-4 to 241)	148 (42 to 289)	15 (-69 to 95)	-47 (-83 to 67)

Statistical analyses

Statistical analysis title	Difference in change from baseline

Statistical analysis description:

Null hypothesis: Changes from baseline through Week 48 in plasma CD4 count for the tenofovir DF and placebo groups are equal. Alternative hypothesis: Changes from baseline through Week 48 in CD4 count for the tenofovir DF and placebo groups are different (two-sided).

Comparison groups	Tenofovir DF v Placebo
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	other[20]
P-value	= 0.47 [21]
Method	Van Elteren test

Notes:

[20] - Intergroup analysis

[21] - No adjustments for multiple comparisons were made. P-value is from a Van Elteren test stratified by baseline GSS (without tenofovir DF) <= or > median (median GSS is 2).

Secondary: Change from baseline to Week 96 in CD4 count

End point title	Change from baseline to Week 96 in CD4 count[22]

End point description:

ITT Analysis Set, missing = excluded method

End point type	Secondary

End point timeframe:

Baseline to 96 weeks

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	20	17	3	
Units: cells/mm3				
median (inter-quartile range (Q1-Q3))	152 (52 to 266)	-6 (-96 to 85)	-69 (-75 to 278)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 144 in CD4 count

End point title	Change from baseline to Week 144 in CD4 count[23]

End point description:

ITT Analysis Set, missing = excluded method

End point type	Secondary

End point timeframe:

Baseline to 144 weeks

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	12	11	2	
Units: cells/mm^3				
median (inter-quartile range (Q1-Q3))	188 (53 to 361)	-88 (-165 to 93)	33 (-109 to 174)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 192 in CD4 count

End point title	Change from baseline to Week 192 in CD4 count[24]

End point description:

ITT Analysis Set, missing = excluded method

End point type	Secondary

End point timeframe:

Baseline to 192 weeks

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	7	6	2	
Units: cells/mm^3				
median (inter-quartile range (Q1-Q3))	166 (-82 to 333)	-70 (-155 to 220)	-23 (-46 to 1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 240 in CD4 count

End point title	Change from baseline to Week 240 in CD4 count[25]

End point description:

ITT Analysis Set, missing = excluded method

End point type	Secondary

End point timeframe:

Baseline to 240 weeks

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	2	1	
Units: cells/mm^3				
median (inter-quartile range (Q1-Q3))	221 (59 to 368)	571 (-13 to 1155)	258 (258 to 258)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 288 in CD4 Count

End point title	Change from Baseline to Week 288 in CD4 Count[26]

End point description:

ITT Analysis Set, missing = excluded method

End point type	Secondary

End point timeframe:

Baseline to 288 weeks

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL

group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	1	1	1	
Units: cells/mm^3				
median (inter-quartile range (Q1-Q3))	310 (310 to 310)	100 (100 to 100)	309 (309 to 309)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 336 in CD4 Count

End point title	Change from Baseline to Week 336 in CD4 Count[27]

End point description:

ITT Analysis Set, missing = excluded method

No analysis was performed because the last study participant discontinued after Week 294 and the study was closed.

End point type	Secondary

End point timeframe:

Baseline to 336 weeks

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[28]	0[29]	0[30]	
Units: cells/mm^3				
median (inter-quartile range (Q1-Q3))	(to)	(to)	(to)	

Notes:

[28] - No analysis was performed because the study ended early after Week 294.

[29] - No analysis was performed because the study ended early after Week 294.

[30] - No analysis was performed because the study ended early after Week 294.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 24 in CD4 Percentage

End point title	Change from baseline to Week 24 in CD4 Percentage

End point description:

ITT Analysis Set, missing = excluded method

CD4 percentage is the percentage of total lymphocytes that are CD4 cells. For the TDF and Placebo groups, only data collected during the double-blind phase are included.

End point type	Secondary

End point timeframe:

Baseline to 24 weeks

End point values	Tenofovir DF	Placebo	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	42	41	18	16
Units: Percentage of CD4 lymphocytes				
median (inter-quartile range (Q1-Q3))	3 (0 to 6)	2 (-1 to 4)	0 (-3 to 3)	-1 (-3 to 2)

Statistical analyses

Statistical analysis title	Difference in change from baseline

Statistical analysis description:

Null hypothesis: Changes from baseline through Week 24 in plasma CD4% for the tenofovir DF and placebo groups are equal. Alternative hypothesis: Changes from baseline through Week 24 in CD4% for the tenofovir DF and placebo groups are different (two-sided).

Comparison groups	Tenofovir DF v Placebo
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other[31]
P-value	= 0.26 [32]
Method	Van Elteren test

Notes:

[31] - Intergroup analysis

[32] - No adjustments for multiple comparisons were made. P-value is from a Van Elteren test stratified by baseline GSS (without tenofovir DF) <= or > median (median GSS is 2).

Secondary: Change from baseline to Week 48 in CD4 Percentage

End point title	Change from baseline to Week 48 in CD4 Percentage

End point description:

ITT Analysis Set, missing = excluded method

CD4 percentage is the percentage of total lymphocytes that are CD4 cells. For the TDF and Placebo groups, only data collected during the double-blind phase are included.

End point type	Secondary

End point timeframe:

Baseline to 48 weeks

End point values	Tenofovir DF	Placebo	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	32	31	17	11
Units: Percentage of CD4 lymphocytes				
median (inter-quartile range (Q1-Q3))	6 (2.5 to 9)	5 (2 to 8)	2 (1 to 4)	-1 (-4 to 7)

Statistical analyses

Statistical analysis title	Difference in change from baseline

Statistical analysis description:

Null hypothesis: Changes from baseline through Week 48 in plasma CD4% for the tenofovir DF and placebo groups are equal. Alternative hypothesis: Changes from baseline through Week 48 in CD4% for the tenofovir DF and placebo groups are different (two-sided).

Comparison groups	Tenofovir DF v Placebo
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	other[33]
P-value	= 0.63 [34]
Method	Van Elteren test

Notes:

[33] - Intergroup analysis

[34] - No adjustments for multiple comparisons were made. P-value is from a Van Elteren test stratified by baseline GSS (without tenofovir DF) <= or > median (median GSS is 2).

Secondary: Change from baseline to Week 96 in CD4 Percentage

End point title	Change from baseline to Week 96 in CD4 Percentage[35]

End point description:

ITT Analysis Set, missing = excluded method

CD4 percentage is the percentage of total lymphocytes that are CD4 cells.

End point type	Secondary

End point timeframe:

Baseline to 96 weeks

Notes:

[35] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	20	17	3	
Units: Percentage of CD4 lymphocytes				
median (inter-quartile range (Q1-Q3))	5 (2 to 8)	2 (0 to 5)	9 (2 to 15)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 144 in CD4 Percentage

End point title	Change from baseline to Week 144 in CD4 Percentage[36]

End point description:

ITT Analysis Set, missing = excluded method

CD4 percentage is the percentage of total lymphocytes that are CD4 cells.

End point type	Secondary

End point timeframe:

Baseline to 144 weeks

Notes:

[36] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	12	11	2	
Units: Percentage of CD4 lymphocytes				
median (inter-quartile range (Q1-Q3))	6.5 (-2 to 13)	0 (-4 to 8)	5.5 (2 to 9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 192 in CD4 Percentage

End point title	Change from baseline to Week 192 in CD4 Percentage[37]

End point description:

ITT Analysis Set, missing = excluded method

CD4 percentage is the percentage of total lymphocytes that are CD4 cells.

End point type	Secondary

End point timeframe:

Baseline to 192 weeks

Notes:

[37] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	7	6	2	
Units: Percentage of CD4 lymphocytes				
median (inter-quartile range (Q1-Q3))	5 (-2 to 11.6)	1.9 (-1 to 10)	4.8 (1.5 to 8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 240 in CD4 Percentage

End point title	Change from baseline to Week 240 in CD4 Percentage[38]

End point description:

ITT Analysis Set, missing = excluded method

CD4 percentage is the percentage of total lymphocytes that are CD4 cells.

End point type	Secondary

End point timeframe:

Baseline to 240 weeks

Notes:

[38] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	2	1	
Units: Percentage of CD4 lymphocytes				
median (inter-quartile range (Q1-Q3))	10 (-2 to 13.3)	8.9 (8.2 to 9.6)	18.9 (18.9 to 18.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 288 in CD4 Percentage

End point title	Change from Baseline to Week 288 in CD4 Percentage[39]

End point description:

ITT Analysis Set, missing = excluded method

CD4 percentage is the percentage of total lymphocytes that are CD4 cells.

End point type	Secondary

End point timeframe:

Baseline to 288 weeks

Notes:

[39] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	1	1	1	
Units: Percentage of CD4 lymphocytes				
median (inter-quartile range (Q1-Q3))	7.4 (7.4 to 7.4)	4 (4 to 4)	11.9 (11.9 to 11.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 336 in CD4 Percentage

End point title	Change from baseline to Week 336 in CD4 Percentage[40]

End point description:

ITT Analysis Set, missing = excluded method

No analysis was performed because the last study participant discontinued after Week 294 and the study was closed.

End point type	Secondary

End point timeframe:

Baseline to 336 weeks

Notes:

[40] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[41]	0[42]	0[43]	
Units: Percentage of CD4 lymphocytes				
median (inter-quartile range (Q1-Q3))	(to)	(to)	(to)	

Notes:

[41] - No analysis was performed because the study ended early after Week 294.

[42] - No analysis was performed because the study ended early after Week 294.

[43] - No analysis was performed because the study ended early after Week 294.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with an HIV-1 RNA decrease of ≥ 1.0 log10 copies/mL from baseline to Week 24

End point title	Percentage of participants with an HIV-1 RNA decrease of ≥ 1.0 log10 copies/mL from baseline to Week 24

End point description:

ITT Analysis Set

The Tenofovir DF and Placebo groups were analyzed using the LOCF method. The Placebo/TDF groups were analyzed using the missing = excluded method. For the TDF and Placebo groups, only data collected during the double-blind phase are included.

End point type	Secondary

End point timeframe:

Baseline to 24 weeks

End point values	Tenofovir DF	Placebo	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	44	41	18	16
Units: Percentage of participants				
number (not applicable)	56.8	51.2	0	12.5

Statistical analyses

Statistical analysis title	Difference in percentage

Statistical analysis description:

Null hypothesis: Percentage of participants who had at least a 1.0 log10 copies/mL decrease from baseline to Week 24 in HIV-1 RNA for the tenofovir DF and placebo groups is equal. Alternative hypothesis: Percentage of participants who had at least a 1.0 log10 copies/mL decrease from baseline to Week 24 in HIV-1 RNA for the tenofovir DF and placebo groups is different (two-sided).

Comparison groups	Tenofovir DF v Placebo

Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	other[44]
P-value	= 0.67 [45]
Method	Fisher exact

Notes:

[44] - Intergroup analysis

[45] - No adjustments for multiple comparisons were made.

Secondary: Percentage of participants with an HIV-1 RNA decrease of ≥ 1.0 log10 copies/mL from baseline to Week 48

End point title	Percentage of participants with an HIV-1 RNA decrease of ≥ 1.0 log10 copies/mL from baseline to Week 48

End point description:

ITT Analysis Set.

The Tenofovir DF and Placebo groups were analyzed using the LOCF method. The Placebo/TDF groups were analyzed using the missing = excluded method. For the TDF and Placebo groups, only data collected during the double-blind phase are included.

End point type	Secondary

End point timeframe:

Baseline to 48 weeks

End point values	Tenofovir DF	Placebo	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	44	41	18	8
Units: Percentage of participants				
number (not applicable)	47.7	53.7	0	0

Statistical analyses

Statistical analysis title	Difference in percentage

Statistical analysis description:

Null hypothesis: Percentage of participants who had at least a 1.0 log10 copies/mL decrease from baseline to Week 48 in HIV-1 RNA for the tenofovir DF and placebo groups is equal. Alternative hypothesis: Percentage of participants who had at least a 1.0 log10 copies/mL decrease from baseline to Week 48 in HIV-1 RNA for the tenofovir
DF and placebo groups is different (two-sided).

Comparison groups	Tenofovir DF v Placebo
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	other[46]
P-value	= 0.67 [47]
Method	Fisher exact

Notes:

[46] - Intergroup analysis

[47] - No adjustments for multiple comparisons were made.

Secondary: Percentage of participants with an HIV-1 RNA decrease of ≥ 1.0 log10 copies/mL from baseline to Week 96

End point title	Percentage of participants with an HIV-1 RNA decrease of ≥ 1.0 log10 copies/mL from baseline to Week 96[48]

End point description:

ITT Analysis Set, missing = excluded method

End point type	Secondary

End point timeframe:

Baseline to 96 weeks

Notes:

[48] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	19	17	3	
Units: Percentage of participants				
number (not applicable)	73.7	5.9	33.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with an HIV-1 RNA decrease of ≥ 1.0 log10 copies/mL from baseline to Week 144

End point title	Percentage of participants with an HIV-1 RNA decrease of ≥ 1.0 log10 copies/mL from baseline to Week 144[49]

End point description:

ITT Analysis Set, missing = excluded method

End point type	Secondary

End point timeframe:

Baseline to 144 weeks

Notes:

[49] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	11	2	
Units: Percentage of participants				
number (not applicable)	90	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with an HIV-1 RNA decrease of ≥ 1.0 log10 copies/mL from baseline to Week 192

End point title	Percentage of participants with an HIV-1 RNA decrease of ≥ 1.0 log10 copies/mL from baseline to Week 192[50]

End point description:

ITT Analysis Set, missing = excluded method

End point type	Secondary

End point timeframe:

Baseline to 192 weeks

Notes:

[50] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	7	5	2	
Units: Percentage of participants				
number (not applicable)	71.4	0	50	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with an HIV-1 RNA decrease of ≥ 1.0 log10 copies/mL from baseline to Week 240

End point title	Percentage of participants with an HIV-1 RNA decrease of ≥ 1.0 log10 copies/mL from baseline to Week 240[51]

End point description:

End point type	Secondary

End point timeframe:

Baseline to 240 weeks

Notes:

[51] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	2	1	
Units: Percentage of participants				
number (not applicable)	100	0	100	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with an HIV-1 RNA Decrease of ≥ 1.0 log10 copies/mL from Baseline to Week 288

End point title	Percentage of Participants with an HIV-1 RNA Decrease of ≥ 1.0 log10 copies/mL from Baseline to Week 288[52]

End point description:

ITT Analysis Set, missing = excluded method

End point type	Secondary

End point timeframe:

Baseline to 288 weeks

Notes:

[52] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	1	1	1	
Units: Percentage of participants				
number (not applicable)	100	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with an HIV-1 RNA decrease of ≥ 1.0 log10 copies/mL from baseline to Week 336

End point title	Percentage of participants with an HIV-1 RNA decrease of ≥ 1.0 log10 copies/mL from baseline to Week 336[53]

End point description:

ITT Analysis Set, missing = excluded method

No analysis was performed because the last study participant discontinued after Week 294 and the study was closed.

End point type	Secondary

End point timeframe:

Baseline to 336 weeks

Notes:

[53] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[54]	0[55]	0[56]	
Units: Percentage of participants				
number (not applicable)				

Notes:

[54] - No analysis was performed because the study ended early after Week 294.

[55] - No analysis was performed because the study ended early after Week 294.

[56] - No analysis was performed because the study ended early after Week 294.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with HIV-1 RNA < 400 copies/mL at Week 24

End point title	Percentage of participants with HIV-1 RNA < 400 copies/mL at Week 24

End point description:

ITT Analysis Set

The Tenofovir DF and Placebo groups were analyzed using the missing = failure method in which participants with missing data were considered to have failed to achieve the endpoint. The Placebo/TDF groups were analyzed using the missing = excluded method. For the TDF and Placebo groups, only data collected during the double-blind phase are included.

End point type	Secondary

End point timeframe:

Week 24

End point values	Tenofovir DF	Placebo	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	44	41	18	16
Units: Percentage of participants				
number (not applicable)	40.9	41.5	83.3	6.3

Statistical analyses

Statistical analysis title	Difference in percentage

Statistical analysis description:

Null hypothesis: Percentage of participants with HIV-1 RNA < 400 copies/mL at Week 24 for the tenofovir DF and placebo groups is equal. Alternative hypothesis: Percentage of participants with HIV-1 RNA < 400 copies/mL at Week 24 for the tenofovir DF and placebo groups is different (two-sided).

Comparison groups	Tenofovir DF v Placebo
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	other[57]
P-value	= 1 [58]
Method	Fisher exact

Notes:

[57] - Intergroup analysis

[58] - No adjustments for multiple comparisons were made.

Secondary: Percentage of participants with HIV-1 RNA < 400 copies/mL at Week 48

End point title	Percentage of participants with HIV-1 RNA < 400 copies/mL at Week 48

End point description:

ITT Analysis Set

The Tenofovir DF and Placebo groups were analyzed using the missing = failure method. The Placebo/TDF groups were analyzed using the missing = excluded method. For the TDF and Placebo groups, only data collected during the double-blind phase are included.

End point type	Secondary

End point timeframe:

Week 48

End point values	Tenofovir DF	Placebo	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	44	41	18	8
Units: Percentage of participants				
number (not applicable)	34.1	43.9	77.8	0

Statistical analyses

Statistical analysis title	Difference in percentage

Statistical analysis description:

Null hypothesis: Percentage of participants with HIV-1 RNA < 400 copies/mL at Week 48 for the tenofovir DF and placebo groups is equal. Alternative hypothesis: Percentage of participants with HIV-1 RNA < 400 copies/mL at Week 48 for the tenofovir DF and placebo groups is different (two-sided).

Comparison groups	Tenofovir DF v Placebo
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	other[59]
P-value	= 0.38 [60]
Method	Fisher exact

Notes:

[59] - Intergroup analysis

[60] - No adjustments for multiple comparisons were made.

Secondary: Percentage of participants with HIV-1 RNA < 400 copies/mL at Week 96

End point title	Percentage of participants with HIV-1 RNA < 400 copies/mL at Week 96[61]

End point description:

ITT Analysis Set, missing = excluded method

End point type	Secondary

End point timeframe:

Week 96

Notes:

[61] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	19	17	3	
Units: Percentage of participants				
number (not applicable)	63.2	70.6	33.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with HIV-1 RNA < 400 copies/mL at Week 144

End point title	Percentage of participants with HIV-1 RNA < 400 copies/mL at Week 144[62]

End point description:

ITT Analysis Set, missing = excluded method

End point type	Secondary

End point timeframe:

Week 144

Notes:

[62] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	11	2	
Units: Percentage of participants				
number (not applicable)	70	72.7	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with HIV-1 RNA < 400 copies/mL at Week 192

End point title	Percentage of participants with HIV-1 RNA < 400 copies/mL at Week 192[63]

End point description:

ITT Analysis Set, missing = excluded method

End point type	Secondary

End point timeframe:

Week 192

Notes:

[63] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	7	5	2	
Units: Percentage of participants				

number (not applicable)	57.1	80	50	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with HIV-1 RNA < 400 copies/mL at Week 240

End point title	Percentage of participants with HIV-1 RNA < 400 copies/mL at Week 240[64]

End point description:

ITT Analysis Set, missing = excluded method

End point type	Secondary

End point timeframe:

Week 240

Notes:

[64] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	2	1	
Units: Percentage of participants				
number (not applicable)	75	100	100	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HIV-1 RNA < 400 copies/mL at Week 288

End point title	Percentage of Participants with HIV-1 RNA < 400 copies/mL at Week 288[65]

End point description:

ITT Analysis Set, missing = excluded method

End point type	Secondary

End point timeframe:

Week 288

Notes:

[65] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	1	1	1	
Units: Percentage of participants				
number (not applicable)	0	100	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with HIV-1 RNA < 400 copies/mL at Week 336

End point title	Percentage of participants with HIV-1 RNA < 400 copies/mL at Week 336[66]

End point description:

ITT Analysis Set, missing = excluded method

No analysis was performed because the last study participant discontinued after Week 294 and the study was closed.

End point type	Secondary

End point timeframe:

Week 336

Notes:

[66] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[67]	0[68]	0[69]	
Units: Percentage of participants				
number (not applicable)				

Notes:

[67] - No analysis was performed because the study ended early after Week 294.

[68] - No analysis was performed because the study ended early after Week 294.

[69] - No analysis was performed because the study ended early after Week 294.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with HIV-1 RNA < 50 copies/mL at Week 24

End point title	Percentage of participants with HIV-1 RNA < 50 copies/mL at Week 24

End point description:

ITT Analysis Set

The Tenofovir DF and Placebo groups were analyzed using the missing = failure method. The Placebo/TDF groups were analyzed using the missing = excluded method. For the TDF and Placebo groups, only data collected during the double-blind phase are included.

End point type	Secondary

End point timeframe:

Week 24

End point values	Tenofovir DF	Placebo	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	44	41	18	16
Units: Percentage of participants				
number (not applicable)	20.5	34.1	77.8	0

Statistical analyses

Statistical analysis title	Difference in percentage

Statistical analysis description:

Null hypothesis: Percentage of participants with HIV-1 RNA < 50 copies/mL at Week 24 for the tenofovir DF and placebo groups is equal. Alternative hypothesis: Percentage of participants with HIV-1 RNA < 50 copies/mL at Week 24 for the tenofovir DF and placebo groups is different (two-sided).

Comparison groups	Tenofovir DF v Placebo
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	other[70]
P-value	= 0.22 [71]
Method	Fisher exact

Notes:

[70] - Intergroup analysis

[71] - No adjustments for multiple comparisons were made.

Secondary: Percentage of participants with HIV-1 RNA < 50 copies/mL at Week 48

End point title	Percentage of participants with HIV-1 RNA < 50 copies/mL at Week 48

End point description:

ITT Analysis Set

The Tenofovir DF and Placebo groups were analyzed using the missing = failure method. The Placebo/TDF groups were analyzed using the missing = excluded method. For the TDF and Placebo groups, only data collected during the double-blind phase are included.

End point type	Secondary

End point timeframe:

Week 48

End point values	Tenofovir DF	Placebo	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	44	41	18	8
Units: Percentage of participants				
number (not applicable)	27.3	36.6	61.1	0

Statistical analyses

Statistical analysis title	Difference in percentage

Statistical analysis description:

Null hypothesis: Percentage of participants with HIV-1 RNA < 50 copies/mL at Week 48 for the tenofovir DF and placebo groups is equal. Alternative hypothesis: Percentage of participants with HIV-1 RNA < 50 copies/mL at Week 48 for the tenofovir DF and placebo groups is different (two-sided).

Comparison groups	Tenofovir DF v Placebo
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	other[72]
P-value	= 0.48 [73]
Method	Fisher exact

Notes:

[72] - Intergroup analysis

[73] - No adjustments for multiple comparisons were made.

Secondary: Percentage of participants with HIV-1 RNA < 50 copies/mL at Week 96

End point title	Percentage of participants with HIV-1 RNA < 50 copies/mL at Week 96[74]

End point description:

ITT Analysis Set, missing = excluded method

End point type	Secondary

End point timeframe:

Week 96

Notes:

[74] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	19	17	3	
Units: Percentage of participants				
number (not applicable)	47.4	58.8	33.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with HIV-1 RNA < 50 copies/mL at Week 144

End point title	Percentage of participants with HIV-1 RNA < 50 copies/mL at Week 144[75]

End point description:

ITT Analysis Set, missing = excluded method

End point type	Secondary

End point timeframe:

Week 144

Notes:

[75] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	11	2	
Units: Percentage of participants				
number (not applicable)	70	45.5	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with HIV-1 RNA < 50 copies/mL at Week 192

End point title	Percentage of participants with HIV-1 RNA < 50 copies/mL at Week 192[76]

End point description:

ITT Analysis Set, missing = excluded method

End point type	Secondary

End point timeframe:

Week 192

Notes:

[76] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	7	5	2	
Units: Percentage of participants				
number (not applicable)	42.9	60	50	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with HIV-1 RNA < 50 copies/mL at Week 240

End point title	Percentage of participants with HIV-1 RNA < 50 copies/mL at Week 240[77]

End point description:

ITT Analysis Set, missing = excluded method

End point type	Secondary

End point timeframe:

Week 240

Notes:

[77] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	2	1	
Units: Percentage of participants				
number (not applicable)	75	100	100	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HIV-1 RNA < 50 copies/mL at Week 288

End point title	Percentage of Participants with HIV-1 RNA < 50 copies/mL at Week 288[78]

End point description:

ITT Analysis Set, missing = excluded method

End point type	Secondary

End point timeframe:

Week 288

Notes:

[78] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	1	1	1	
Units: Percentage of participants				
number (not applicable)	0	100	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with HIV-1 RNA < 50 copies/mL at Week 336

End point title	Percentage of participants with HIV-1 RNA < 50 copies/mL at Week 336[79]

End point description:

ITT Analysis Set, missing = excluded method

No analysis was performed because the last study participant discontinued after Week 294 and the study was closed.

End point type	Secondary

End point timeframe:

Week 336

Notes:

[79] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For participants randomized to placebo, results after switching to TDF are presented in the Placebo/TDF, HIV-1 RNA < 1000 Copies/mL group, and the Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL group.

End point values	Tenofovir DF	Placebo/TDF, HIV-1 RNA < 1000 Copies/mL	Placebo/TDF, HIV-1 RNA ≥ 1000 Copies/mL	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[80]	0[81]	0[82]	
Units: Percentage of participants				
number (not applicable)				

Notes:

[80] - No analysis was performed because the study ended early after Week 294.

[81] - No analysis was performed because the study ended early after Week 294.

[82] - No analysis was performed because the study ended early after Week 294.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Virologic Failure through Week 48

End point title	Percentage of Participants with Virologic Failure through Week 48

End point description:

Virologic failure was defined as either nonresponse or viral rebound.
- Nonresponse (failure to achieve response). Response was defined as either
-- A ≥ 0.5 log10 copies/mL decrease in HIV-1 RNA from baseline at 2 consecutive visits, or
-- HIV-1 RNA < 400 copies/mL at 2 consecutive visits.
- Viral rebound was defined as either
-- Participants who achieved a ≥ 0.5 log10 copies/mL decrease from baseline in plasma HIV-1 RNA at 2 consecutive visits, who then subsequently achieved plasma HIV-1 RNA values ≥ 1.0 log10 copies/mL above their on-study nadir (lowest value) and/or plasma HIV-1 RNA values ≥ the baseline value at 2 consecutive visits, or
-- Participants who achieved plasma HIV-1 RNA levels of < 400 copies/mL at 2 consecutive visits, and then subsequently had plasma HIV-1 RNA levels > 1000 copies/mL at 2 consecutive visits.

The virologic failure rate was estimated from Kaplan-Meier product limit method by including all HIV-1 RNA data collected during the double-blind phase.

End point type	Secondary

End point timeframe:

Up to 48 weeks. 1 participant without time to respond (6 days of treatment) was excluded. Nonresponders=failures@time 0. Rebounders=failures on study day of first of 2 assessments meeting criteria. Otherwise, censored at last double-blind HIV measurement.

End point values	Tenofovir DF	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	41		
Units: Kaplan-Meier percentage				
number (not applicable)	51	39		

Statistical analyses

Statistical analysis title	Difference in percentage

Statistical analysis description:

Null hypothesis: The survival functions for the tenofovir DF and placebo groups up to Week 48 are equal.
Alternative hypothesis: The survival functions for the tenofovir DF
and placebo groups up to Week 48 are different (two-sided).

Comparison groups	Tenofovir DF v Placebo

Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	other[83]
P-value	= 0.29 [84]
Method	Logrank

Notes:

[83] - Intergroup analysis

[84] - No adjustments for multiple comparisons were made.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Week 294 plus 30 days.

Adverse event reporting additional description:

Safety Analysis Set: participants were randomized and received at least 1 dose of study medication. MedDRA version 11.1 was used for the Tenofovir DF and Placebo columns; MedDRA version 16.1 was used for the All TDF column.

All AEs are reported by system order class and preferred term.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Tenofovir DF

Reporting group description:

Adverse events occurring in the double-blind phase are presented for this reporting group.

TDF+OBR from baseline to Week 48 (double-blind phase), followed by open-label TDF+ OBR for up to an additional 288 weeks.

Reporting group title	Placebo

Reporting group description:

Adverse events occurring in the double-blind phase are presented for this reporting group.

Placebo to match TDF+OBR from baseline to Week 48 (double-blind phase), followed by open-label TDF+OBR for up to an additional 288 weeks.

Reporting group title	All TDF

Reporting group description:

Adverse events reported for the All TDF group include those reported during the double-blind phase and/or extension phase for subjects who were randomized to TDF group plus adverse events reported during the extension phase only for subjects who switched from placebo to open-label TDF.

Serious adverse events	Tenofovir DF	Placebo	All TDF
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 45 (22.22%)	3 / 42 (7.14%)	20 / 81 (24.69%)
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)			
Anogenital warts			
subjects affected / exposed	0 / 45 (0.00%)	0 / 42 (0.00%)	1 / 81 (1.23%)
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			

Overdose			
subjects affected / exposed	0 / 45 (0.00%)	0 / 42 (0.00%)	1 / 81 (1.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Convulsion			
subjects affected / exposed	1 / 45 (2.22%)	0 / 42 (0.00%)	1 / 81 (1.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 42 (0.00%)	1 / 81 (1.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Psychotic disorder			
subjects affected / exposed	0 / 45 (0.00%)	0 / 42 (0.00%)	1 / 81 (1.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 45 (0.00%)	0 / 42 (0.00%)	1 / 81 (1.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	1 / 45 (2.22%)	0 / 42 (0.00%)	1 / 81 (1.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	3 / 45 (6.67%)	1 / 42 (2.38%)	5 / 81 (6.17%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			

subjects affected / exposed	2 / 45 (4.44%)	0 / 42 (0.00%)	2 / 81 (2.47%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 45 (0.00%)	0 / 42 (0.00%)	3 / 81 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cryptococcosis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 42 (0.00%)	1 / 81 (1.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 42 (0.00%)	1 / 81 (1.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jiroveci pneumonia			
subjects affected / exposed	2 / 45 (4.44%)	0 / 42 (0.00%)	0 / 81 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 42 (0.00%)	2 / 81 (2.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	1 / 45 (2.22%)	0 / 42 (0.00%)	1 / 81 (1.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 45 (2.22%)	0 / 42 (0.00%)	1 / 81 (1.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess			

subjects affected / exposed	0 / 45 (0.00%)	0 / 42 (0.00%)	1 / 81 (1.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess limb			
subjects affected / exposed	0 / 45 (0.00%)	0 / 42 (0.00%)	1 / 81 (1.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 42 (2.38%)	0 / 81 (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
Mastoiditis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 42 (2.38%)	0 / 81 (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
Neurocryptococcosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 42 (0.00%)	1 / 81 (1.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 42 (0.00%)	1 / 81 (1.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral toxoplasmosis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 42 (2.38%)	0 / 81 (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

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

Non-serious adverse events	Tenofovir DF	Placebo	All TDF
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 45 (97.78%)	35 / 42 (83.33%)	76 / 81 (93.83%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 45 (0.00%)	3 / 42 (7.14%)	2 / 81 (2.47%)
occurrences (all)	0	4	2
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 45 (13.33%)	5 / 42 (11.90%)	16 / 81 (19.75%)
occurrences (all)	8	7	21
Dizziness			
subjects affected / exposed	8 / 45 (17.78%)	5 / 42 (11.90%)	11 / 81 (13.58%)
occurrences (all)	9	8	13
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	4 / 45 (8.89%)	1 / 42 (2.38%)	7 / 81 (8.64%)
occurrences (all)	10	1	16
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	4 / 45 (8.89%)	5 / 42 (11.90%)	7 / 81 (8.64%)
occurrences (all)	4	8	9
Eye disorders			
Conjunctivitis			
subjects affected / exposed	2 / 45 (4.44%)	1 / 42 (2.38%)	5 / 81 (6.17%)
occurrences (all)	2	1	5
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	16 / 45 (35.56%)	5 / 42 (11.90%)	21 / 81 (25.93%)
occurrences (all)	21	5	28
Diarrhoea			
subjects affected / exposed	10 / 45 (22.22%)	4 / 42 (9.52%)	17 / 81 (20.99%)
occurrences (all)	10	5	18
Nausea			
subjects affected / exposed	11 / 45 (24.44%)	3 / 42 (7.14%)	15 / 81 (18.52%)
occurrences (all)	14	6	18
Abdominal pain			

subjects affected / exposed	8 / 45 (17.78%)	5 / 42 (11.90%)	9 / 81 (11.11%)
occurrences (all)	8	5	9
Gastritis			
subjects affected / exposed	5 / 45 (11.11%)	1 / 42 (2.38%)	7 / 81 (8.64%)
occurrences (all)	5	1	9
Constipation			
subjects affected / exposed	3 / 45 (6.67%)	0 / 42 (0.00%)	4 / 81 (4.94%)
occurrences (all)	3	0	5
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	3 / 45 (6.67%)	3 / 42 (7.14%)	4 / 81 (4.94%)
occurrences (all)	4	4	5
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	11 / 45 (24.44%)	6 / 42 (14.29%)	24 / 81 (29.63%)
occurrences (all)	13	6	29
Bronchospasm			
subjects affected / exposed	3 / 45 (6.67%)	2 / 42 (4.76%)	5 / 81 (6.17%)
occurrences (all)	3	2	5
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 45 (2.22%)	0 / 42 (0.00%)	7 / 81 (8.64%)
occurrences (all)	1	0	7
Musculoskeletal and connective tissue disorders			
Osteopenia			
subjects affected / exposed	3 / 45 (6.67%)	2 / 42 (4.76%)	5 / 81 (6.17%)
occurrences (all)	3	2	5
Infections and infestations			
Sinusitis			
subjects affected / exposed	12 / 45 (26.67%)	6 / 42 (14.29%)	24 / 81 (29.63%)
occurrences (all)	14	6	31
Nasopharyngitis			
subjects affected / exposed	8 / 45 (17.78%)	7 / 42 (16.67%)	18 / 81 (22.22%)
occurrences (all)	10	10	34
Upper respiratory tract infection			

subjects affected / exposed	8 / 45 (17.78%)	3 / 42 (7.14%)	17 / 81 (20.99%)
occurrences (all)	13	4	25
Tonsillitis			
subjects affected / exposed	4 / 45 (8.89%)	3 / 42 (7.14%)	12 / 81 (14.81%)
occurrences (all)	4	4	13
Oral herpes			
subjects affected / exposed	5 / 45 (11.11%)	3 / 42 (7.14%)	9 / 81 (11.11%)
occurrences (all)	7	3	12
Tracheobronchitis			
subjects affected / exposed	5 / 45 (11.11%)	1 / 42 (2.38%)	9 / 81 (11.11%)
occurrences (all)	6	1	11
Acute sinusitis			
subjects affected / exposed	3 / 45 (6.67%)	4 / 42 (9.52%)	6 / 81 (7.41%)
occurrences (all)	5	4	9
Rhinitis			
subjects affected / exposed	3 / 45 (6.67%)	1 / 42 (2.38%)	7 / 81 (8.64%)
occurrences (all)	3	1	8
Pneumonia			
subjects affected / exposed	2 / 45 (4.44%)	2 / 42 (4.76%)	5 / 81 (6.17%)
occurrences (all)	2	3	5
Body tinea			
subjects affected / exposed	2 / 45 (4.44%)	1 / 42 (2.38%)	5 / 81 (6.17%)
occurrences (all)	2	1	5
Furuncle			
subjects affected / exposed	3 / 45 (6.67%)	1 / 42 (2.38%)	4 / 81 (4.94%)
occurrences (all)	4	1	5
Gastroenteritis			
subjects affected / exposed	2 / 45 (4.44%)	1 / 42 (2.38%)	5 / 81 (6.17%)
occurrences (all)	2	1	5
Bronchopneumonia			
subjects affected / exposed	2 / 45 (4.44%)	0 / 42 (0.00%)	5 / 81 (6.17%)
occurrences (all)	2	0	5
Hordeolum			
subjects affected / exposed	3 / 45 (6.67%)	1 / 42 (2.38%)	3 / 81 (3.70%)
occurrences (all)	3	1	3
Impetigo			

subjects affected / exposed	1 / 45 (2.22%)	3 / 42 (7.14%)	3 / 81 (3.70%)
occurrences (all)	1	3	3
Herpes zoster			
subjects affected / exposed	0 / 45 (0.00%)	3 / 42 (7.14%)	3 / 81 (3.70%)
occurrences (all)	0	3	4
Metabolism and nutrition disorders			
Hypertriglyceridaemia			
subjects affected / exposed	3 / 45 (6.67%)	3 / 42 (7.14%)	6 / 81 (7.41%)
occurrences (all)	3	3	7
Anorexia			
subjects affected / exposed	4 / 45 (8.89%)	1 / 42 (2.38%)	0 / 81 (0.00%)
occurrences (all)	4	1	0
Decreased appetite			
subjects affected / exposed	0 / 45 (0.00%)	0 / 42 (0.00%)	5 / 81 (6.17%)
occurrences (all)	0	0	6

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 October 2006	An independent data monitoring committee was added to participate in the review of the efficacy and safety profile for the study.
21 February 2007	The study was extended to 144 weeks with the addition of a 96-week, open-label extension period.
04 November 2008	The study was extended to 240 weeks with the addition of a second 96-week, open-label extension period.
03 September 2010	The study was extended for an additional 2 years. After completing the second 96-week study extension with open-label tenofovir DF, currently enrolled subjects at active sites who had not yet reached 18 years of age and who had shown benefit from tenofovir DF were given the option to continue receiving tenofovir DF for an additional 96 weeks. For subjects completing the extension phase, tenofovir DF was provided until the subject reached 18 years of age, until tenofovir DF became commercially available in the country in which the subject was enrolled, or until Gilead was no longer the exclusive seller of tenofovir DF in the country in which the subject was enrolled, whichever occured first.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Participants left the study for a number of reasons (eg, turned 18 years old, switched to a different HIV treatment regimen), which led to small numbers of participants analyzed at later time points, and the study was concluded earlier than planned.

Notes: