Clinical trial results:
A Phase III, Randomised, Open- Label Study Comparing the Safety and Efficacy of Switching Stavudine or Zidovudine to Tenofovir Disoproxil Fumarate versus Continuing Stavudine or Zidovudine in Virologically Suppressed HIV-Infected Children Taking Highly Active Antiretroviral Therapy

Summary

EudraCT number	2007-003418-32
Trial protocol	GB Outside EU/EEA
Global end of trial date	16 August 2017

Results information

Result version number	v1 (current)
This version publication date	02 March 2018
First version publication date	02 March 2018

Trial information

Trial identification

Sponsor protocol code	GS-US-104-0352

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00528957
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 Trials Mailbox, Gilead Sciences International Ltd, GileadClinicalTrials@gilead.com
Scientific contact	Clinical Trials Mailbox, Gilead Sciences International Ltd, GileadClinicalTrials@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	16 August 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 April 2009
Global end of trial reached?	Yes
Global end of trial date	16 August 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to assess the efficacy of switching to tenofovir disoproxil fumarate (TDF) compared to continuing stavudine or zidovudine in maintaining virologic suppression in HIV-1 infected children.

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: -

Evidence for comparator: -

Actual start date of recruitment	28 December 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	United Kingdom: 3
Country: Number of subjects enrolled	United States: 22
Country: Number of subjects enrolled	Panama: 72
Worldwide total number of subjects	97
EEA total number of subjects	3

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23	0

months)	
Children (2-11 years)	92
Adolescents (12-17 years)	5
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in the United States, Panama, and the United Kingdom. The first participant was screened on 28 December 2006. The last study visit occurred on 16 August 2017.

Pre-assignment

Screening details:

127 participants were screened.

Period 1

Period 1 title	Randomized Phase (Baseline to Week 48)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Tenofovir DF

Arm description:

Participants in this group received tenofovir disoproxil fumarate (TDF) during the randomized phase (48 weeks).

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

Dosage and administration details:

300 mg tablets for participants > 37 kg; 8 mg/kg oral powder (up to 300 mg) for participants ≤ 37 kg

Arm title	Stavudine or Zidovudine

Arm description:

Participants in this group received stavudine or zidovudine during the randomized phase (48 weeks).

Arm type	Active comparator
Investigational medicinal product name	Zidovudine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution, Capsule
Routes of administration	Oral use

Dosage and administration details:

Zidovudine as prescribed by the investigator prior to study entry (pediatric participants < 30 kg: 1 mg/kg/dose given every 12 hours; pediatric participants ≥ 30 kg: 30 mg twice daily)

Investigational medicinal product name	Stavudine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Oral solution
Routes of administration	Oral use

Dosage and administration details:

Stavudine as prescribed by the investigator prior to study entry (pediatric participants 6 weeks to 12 years of age: 160 mg/m^2 every 8 hours; pediatric participants > 12 years of age: 300 mg twice daily)

Number of subjects in period 1	Tenofovir DF	Stavudine or Zidovudine
Started	48	49
Completed	44	48
Not completed	4	1
Withdrew Consent	2	1
Safety, Tolerability, or Efficacy Reason	2	-

Period 2

Period 2 title	First Extension (Week 48 to Week 144)
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Tenofovir DF

Arm description:

Participants in this group received TDF after receiving TDF during the randomized phase.

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

Dosage and administration details:

300 mg tablets for participants > 37 kg; 8 mg/kg oral powder (up to 300 mg) for participants ≤ 37 kg

Arm title	Stavudine or Zidovudine

Arm description:

Participants in this group received TDF after receiving stavudine or zidovudine during the randomized phase.

Arm type	Active comparator
Investigational medicinal product name	Tenofovir disoproxil fumarate
Investigational medicinal product code	
Other name	TDF, Viread®
Pharmaceutical forms	Oral powder, Tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg tablets for participants > 37 kg; 8 mg/kg oral powder (up to 300 mg) for participants ≤ 37 kg

Number of subjects in period 2[1]	Tenofovir DF	Stavudine or Zidovudine
Started	38	41
Completed	35	40
Not completed	3	1
Withdrew Consent	-	1
Investigator's Discretion	2	-
Safety, Tolerability, or Efficacy Reason	1	-

Notes:

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

Justification: 13 participants (6 from TDF; 7 from Stavudine or Zidovudine) completed the 48-week randomized phase and did not enroll in the first extension.

Period 3

Period 3 title	Second Extension (Week 144 to Week 240)
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Tenofovir DF

Arm description:

Participants in this group received TDF after receiving TDF in the randomized phase.

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

Dosage and administration details:

300 mg tablets for participants > 37 kg; 8 mg/kg oral powder (up to 300 mg) for participants ≤ 37 kg

Arm title	Stavudine or Zidovudine

Arm description:

Participants in this group received TDF after receiving stavudine or zidovudine during the randomized phase.

Arm type	Active comparator
Investigational medicinal product name	Tenofovir disoproxil fumarate
Investigational medicinal product code	
Other name	TDF, Viread®
Pharmaceutical forms	Oral powder, Tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg tablets for participants > 37 kg; 8 mg/kg oral powder (up to 300 mg) for participants ≤ 37 kg

Number of subjects in period 3[2]	Tenofovir DF	Stavudine or Zidovudine
Started	34	40
Completed	27	37
Not completed	7	3
Investigator's Discretion	3	-
Safety, Tolerability, or Efficacy Reason	4	3

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: 1 participant from the TDF group completed the first extension and did not enroll in the second extension.

Period 4

Period 4 title	Third Extension (Week 240 to Week 336)
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Tenofovir DF

Arm description:

Participants in this group received TDF after receiving TDF during the randomized phase.

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

Dosage and administration details:

300 mg tablets for participants > 37 kg; 8 mg/kg oral powder (up to 300 mg) for participants ≤ 37 kg

Arm title	Stavudine or Zidovudine

Arm description:

Participants in this group received TDF after receiving stavudine or zidovudine during the randomized phase.

Arm type	Active comparator
Investigational medicinal product name	Tenofovir disoproxil fumarate
Investigational medicinal product code	
Other name	TDF, Viread®
Pharmaceutical forms	Oral powder, Tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg tablets for participants > 37 kg; 8 mg/kg oral powder (up to 300 mg) for participants ≤ 37 kg

Number of subjects in period 4	Tenofovir DF	Stavudine or Zidovudine
Started	27	37
Completed	21	27
Not completed	6	10
Withdrew Consent	-	1
= 18 yr old & TDF approved in adults	1	1
Investigator's Discretion	-	1
Lost to follow-up	-	3
Safety, Tolerability, or Efficacy Reason	5	4

Period 5	
Period 5 title	Long-Term Extension (Week 336 and On)
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Tenofovir DF

Arm description:

Participants in this group received TDF after receiving TDF during the randomized phase.

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

Dosage and administration details:

300 mg tablets for participants > 37 kg; 8 mg/kg oral powder (up to 300 mg) for participants ≤ 37 kg

Arm title	Stavudine or Zidovudine

Arm description:

Participants in this group received TDF after receiving stavudine or zidovudine during the randomized phase.

Arm type	Active comparator
Investigational medicinal product name	Tenofovir disoproxil fumarate
Investigational medicinal product code	
Other name	TDF, Viread®
Pharmaceutical forms	Oral powder, Tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg tablets for participants > 37 kg; 8 mg/kg oral powder (up to 300 mg) for participants ≤ 37 kg

Number of subjects in period 5[3]	Tenofovir DF	Stavudine or Zidovudine
Started	19	25
Completed	9	8
Not completed	10	17
Withdrew Consent	2	1
Rolled Over to Study GS-US-311-1269	4	10
Investigator's Discretion	1	1
Safety, Tolerability, or Efficacy Reason	3	5

Notes:

[3] - 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: 4 participants (2 from TDF; 2 from Stavudine or Zidovudine) completed the third extension and did not enroll in the long-term extension.

Baseline characteristics

Reporting groups	
Reporting group title	Tenofovir DF
Reporting group description:	
Participants in this group received tenofovir disoproxil fumarate (TDF) during the randomized phase (48 weeks).	
Reporting group title	Stavudine or Zidovudine
Reporting group description:	
Participants in this group received stavudine or zidovudine during the randomized phase (48 weeks).	

Reporting group values	Tenofovir DF	Stavudine or Zidovudine	Total
Number of subjects	48	49	97
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	7	7	
standard deviation	± 3.3	± 2.6	-
Gender categorical Units: Subjects			
Female	27	20	47
Male	21	29	50
Ethnicity Units: Subjects			
Hispanic or Latino	35	42	77
Not Hispanic or Latino	13	7	20
Race Units: Subjects			
American Indian or Alaska Native	2	0	2
Asian	1	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	13	6	19
White	3	6	9
Mestizo	28	37	65
Native Indian (Kuna)	1	0	1
Plasma HIV-1 RNA Units: Subjects			
< 50 copies/ mL	36	41	77
50 to < 400 copies/mL	11	6	17
400 to < 1000 copies/ mL	1	1	2
≥ 1000 copies/mL	0	1	1
Height Units: cm			
arithmetic mean	118	119	
standard deviation	± 19.8	± 16.7	-
Body Mass Index			

Units: kg/m^2			
arithmetic mean	17.59	16.59	
standard deviation	± 3.680	± 1.762	-
Weight			
Units: kilograms			
arithmetic mean	25.9	24.1	
standard deviation	± 12.03	± 7.77	-
CD4 Cell Count			
Units: cells/mm^3			
arithmetic mean	1190	1144	
standard deviation	± 541.7	± 388.4	-
CD4 Percentage			
Units: percentage			
arithmetic mean	33.9	33.0	
standard deviation	± 7.44	± 6.82	-

End points

End points reporting groups

Reporting group title	Tenofovir DF
Reporting group description:	
Participants in this group received tenofovir disoproxil fumarate (TDF) during the randomized phase (48 weeks).	
Reporting group title	Stavudine or Zidovudine
Reporting group description:	
Participants in this group received stavudine or zidovudine during the randomized phase (48 weeks).	
Reporting group title	Tenofovir DF
Reporting group description:	
Participants in this group received TDF after receiving TDF during the randomized phase.	
Reporting group title	Stavudine or Zidovudine
Reporting group description:	
Participants in this group received TDF after receiving stavudine or zidovudine during the randomized phase.	
Reporting group title	Tenofovir DF
Reporting group description:	
Participants in this group received TDF after receiving TDF in the randomized phase.	
Reporting group title	Stavudine or Zidovudine
Reporting group description:	
Participants in this group received TDF after receiving stavudine or zidovudine during the randomized phase.	
Reporting group title	Tenofovir DF
Reporting group description:	
Participants in this group received TDF after receiving TDF during the randomized phase.	
Reporting group title	Stavudine or Zidovudine
Reporting group description:	
Participants in this group received TDF after receiving stavudine or zidovudine during the randomized phase.	
Reporting group title	Tenofovir DF
Reporting group description:	
Participants in this group received TDF after receiving TDF during the randomized phase.	
Reporting group title	Stavudine or Zidovudine
Reporting group description:	
Participants in this group received TDF after receiving stavudine or zidovudine during the randomized phase.	
Subject analysis set title	(Stavudine or Zidovudine)/TDF
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants in this group received stavudine or zidovudine during the randomized phase (48 weeks) and then received TDF during the extension phase(s).	
Subject analysis set title	All TDF
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All participants who received tenofovir DF in the randomized and/or extension phases	

Primary: 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:

This is the percentage of participants with HIV-1 RNA < 400 copies/mL after 48 weeks of exposure to randomized study drug. The Intent-to-Treat (ITT) Analysis Set included all participants who were randomized and received at least one dose of study drug. Missing = Failure.

End point type	Primary

End point timeframe:

48 weeks

End point values	Tenofovir DF	Stavudine or Zidovudine	All TDF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	48	49	89	
Units: percentage of participants				
number (not applicable)	83.3	91.8	85.4	

Statistical analyses

Statistical analysis title	Statistical Analysis - TDF vs Stavudine/Zidovudine

Statistical analysis description:

The statistical hypotheses for the primary endpoint was as follows:
• Null Hypothesis: tenofovir DF group is more than 15% worse than the stavudine or zidovudine group with respect to the proportion of participants maintaining HIV-1 RNA concentrations < 400 copies/mL at Week 48.
• Alternate Hypothesis: tenofovir DF group is no more than 15% worse than the stavudine or zidovudine group with respect to the proportion of participants maintaining HIV-1 RNA < 400 copies/mL at Week 48.

Comparison groups	Tenofovir DF v Stavudine or Zidovudine
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in percentages between groups
Point estimate	-8.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.5
upper limit	4.5

Notes:

[1] - In the randomized phase, it was assumed that the respective proportions of participants maintaining HIV-1 RNA < 400 copies/mL was 92% for participants switching to tenofovir DF and 90% for participants continuing stavudine or zidovudine, as estimated from previous GSI studies. The equivalence limit was set at −15% for the lower boundary of a two-sided 95% confidence interval (CI) on the difference in proportions of participants maintaining HIV-1 RNA < 400 copies/mL at Week 48.

Secondary: Virologic Success at 48 Weeks (HIV-1 RNA Cutoff at 400 Copies/mL, Snapshot)

End point title	Virologic Success at 48 Weeks (HIV-1 RNA Cutoff at 400 Copies/mL, Snapshot)

End point description:

This is the percentage of participants with virologic success after 48 weeks of exposure to randomized study drug. Participants from the Intent-to-Treat (ITT) Analysis Set who were less than 12 years of age at baseline were analyzed. The percentage of participants achieving HIV-1 RNA < 400 copies/mL at Week 48 was analyzed using the snapshot algorithm, which defines a patient's virologic response status using only the viral load at the predefined time point within an allowed window of time, along with study drug discontinuation status.

End point type	Secondary

End point timeframe:

48 weeks

End point values	Tenofovir DF	Stavudine or Zidovudine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	48		
Units: percentage of participants				
number (not applicable)	88.6	89.6		

Statistical analyses

Statistical analysis title	Virologic Success at 48 Weeks

Statistical analysis description:

In the randomized phase, it was assumed that the respective proportions of participants maintaining HIV-1 RNA < 400 copies/mL was 92% for subjects switching to tenofovir DF
and 90% for subjects continuing stavudine or zidovudine, as estimated from previous GSI studies. The equivalence limit was set at −15% for the lower boundary of a two-sided 95%
confidence interval (CI) on the difference in proportions of participants maintaining HIV-1 RNA < 400 copies/mL at Week 48.

Comparison groups	Tenofovir DF v Stavudine or Zidovudine
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Difference in percentages between groups
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.7
upper limit	11.8

Notes:

[2] - The difference between the two proportions and its CI were based on normal approximation methods.

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

End point description:

This is the percentage of participants with HIV-1 RNA < 400 copies/mL after 96 weeks of exposure to

TDF. Intent-to-treat, Missing = Failure. Participants who had not reached the upper limit of the analysis window (date varies depending on analysis time frame) were excluded.

End point type	Secondary

End point timeframe:

96 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	38	41	79	
Units: percentage of participants				
number (not applicable)	81.6	85.4	83.5	

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

End point description:

This is the percentage of participants with HIV-1 RNA < 400 copies/mL after 144 weeks of exposure to TDF. Intent-to-treat, Missing = Failure. Participants who had not reached the upper limit of the analysis window (date varies depending on analysis time frame) were excluded.

End point type	Secondary

End point timeframe:

144 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	38	40	78	
Units: percentage of participants				
number (not applicable)	73.7	87.5	80.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 400 Copies/mL at 192 Weeks

End point title	Percentage of Participants With HIV-1 RNA < 400 Copies/mL at 192 Weeks

End point description:

This is the percentage of participants with HIV-1 RNA < 400 copies/mL after 192 weeks of exposure to TDF. Intent-to-treat, Missing = Failure. Participants who had not reached the upper limit of the analysis window (date varies depending on analysis time frame) were excluded.

End point type	Secondary

End point timeframe:

192 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	34	40	74	
Units: percentage of participants				
number (not applicable)	70.6	82.5	77.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 400 Copies/mL at 240 Weeks

End point title	Percentage of Participants With HIV-1 RNA < 400 Copies/mL at 240 Weeks

End point description:

This is the percentage of participants with HIV-1 RNA < 400 copies/mL after 240 weeks of exposure to TDF. Intent-to-treat, Missing = Failure. Participants who had not reached the upper limit of the analysis window (date varies depending on analysis time frame) were excluded.

End point type	Secondary

End point timeframe:

240 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	34	37	71	
Units: percentage of participants				
number (not applicable)	70.6	75.7	73.2	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 400 Copies/mL at 288 Weeks

End point title	Percentage of Participants With HIV-1 RNA < 400 Copies/mL at 288 Weeks

End point description:

This is the percentage of participants with HIV-1 RNA < 400 copies/mL after 288 weeks of exposure to TDF. Intent-to-treat, Missing = Failure. Participants who had not reached the upper limit of the analysis window (date varies depending on analysis time frame) were excluded.

End point type	Secondary

End point timeframe:

288 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	27	37	64	
Units: percentage of participants				
number (not applicable)	81.5	67.6	73.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 400 Copies/mL at 336 Weeks

End point title	Percentage of Participants With HIV-1 RNA < 400 Copies/mL at 336 Weeks

End point description:

This is the percentage of participants with HIV-1 RNA < 400 copies/mL after 336 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

336 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	21	43	
Units: percentage of participants				
number (not applicable)	90.9	100.0	95.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 400 Copies/mL at 384 Weeks

End point title	Percentage of Participants With HIV-1 RNA < 400 Copies/mL at 384 Weeks

End point description:

This is the percentage of participants with HIV-1 RNA < 400 copies/mL after 384 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

384 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	17	9	26	
Units: percentage of participants				
number (not applicable)	100.0	100.0	100.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 400 Copies/mL at 432 Weeks

End point title	Percentage of Participants With HIV-1 RNA < 400 Copies/mL at 432 Weeks

End point description:

This is the percentage of participants with HIV-1 RNA < 400 copies/mL after 432 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

432 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	13	7	20	
Units: percentage of participants				
number (not applicable)	100.0	85.7	95.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 400 Copies/mL at 480 Weeks

End point title	Percentage of Participants With HIV-1 RNA < 400 Copies/mL at 480 Weeks

End point description:

This is the percentage of participants with HIV-1 RNA < 400 copies/mL after 480 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

480 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	9	2	11	
Units: percentage of participants				
number (not applicable)	88.9	100.0	90.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 400 Copies/mL at 528 Weeks

End point title	Percentage of Participants With HIV-1 RNA < 400 Copies/mL at 528 Weeks

End point description:

This is the percentage of participants with HIV-1 RNA < 400 copies/mL after 528 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

528 weeks

End point values	Tenofovir DF	All TDF		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	6	6		
Units: percentage of participants				
number (not applicable)	100.0	100.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at 48 Weeks

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at 48 Weeks

End point description:

This is the percentage of participants with HIV-1 RNA < 50 copies/mL after 48 weeks of exposure to randomized study drug. Intent-to-treat, Missing = Failure. Participants who had not reached the upper limit of the analysis window (date varies depending on analysis time frame) were excluded.

End point type	Secondary

End point timeframe:

48 weeks

End point values	Tenofovir DF	Stavudine or Zidovudine	All TDF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	48	49	89	
Units: percentage of participants				
number (not applicable)	70.8	85.7	68.5	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at 96 Weeks

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at 96 Weeks

End point description:

This is the percentage of participants with HIV-1 RNA < 50 copies/mL after 96 weeks of exposure to TDF. Intent-to-treat, Missing = Failure. Participants who had not reached the upper limit of the analysis window (date varies depending on analysis time frame) were excluded.

End point type	Secondary

End point timeframe:

96 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	38	41	79	
Units: percentage of participants				
number (not applicable)	76.3	68.3	72.2	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at 144 Weeks

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at 144 Weeks

End point description:

This is the percentage of participants with HIV-1 RNA < 50 copies/mL after 144 weeks of exposure to TDF. Intent-to-treat, Missing = Failure. Participants who had not reached the upper limit of the analysis window (date varies depending on analysis time frame) were excluded.

End point type	Secondary

End point timeframe:

144 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	38	40	78	
Units: percentage of participants				
number (not applicable)	63.2	75.0	69.2	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at 192 Weeks

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at 192 Weeks

End point description:

This is the percentage of participants with HIV-1 RNA < 50 copies/mL after 192 weeks of exposure to TDF. Intent-to-treat, Missing = Failure. Participants who had not reached the upper limit of the analysis

window (date varies depending on analysis time frame) were excluded.

End point type	Secondary

End point timeframe:

192 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	34	40	74	
Units: percentage of participants				
number (not applicable)	67.6	75.0	71.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at 240 Weeks

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at 240 Weeks

End point description:

This is the percentage of participants with HIV-1 RNA < 50 copies/mL after 240 weeks of exposure to TDF. Intent-to-treat, Missing = Failure. Participants who had not reached the upper limit of the analysis window (date varies depending on analysis time frame) were excluded.

End point type	Secondary

End point timeframe:

240 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	34	37	71	
Units: percentage of participants				
number (not applicable)	70.6	73.0	71.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at 288 Weeks

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at 288 Weeks

End point description:

This is the percentage of participants with HIV-1 RNA < 50 copies/mL after 288 weeks of exposure to TDF. Intent-to-treat, Missing = Failure. Participants who had not reached the upper limit of the analysis window (date varies depending on analysis time frame) were excluded.

End point type	Secondary

End point timeframe:

288 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	27	37	64	
Units: percentage of participants				
number (not applicable)	81.5	62.2	70.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at 336 Weeks

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at 336 Weeks

End point description:

This is the percentage of participants with HIV-1 RNA < 50 copies/mL after 336 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

336 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	21	43	
Units: percentage of participants				
number (not applicable)	86.4	90.5	88.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at 384 Weeks

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at 384 Weeks

End point description:

This is the percentage of participants with HIV-1 RNA < 50 copies/mL after 384 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

384 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	17	9	26	
Units: percentage of participants				
number (not applicable)	88.2	100.0	92.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at 432 Weeks

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at 432 Weeks

End point description:

This is the percentage of participants with HIV-1 RNA < 50 copies/mL after 432 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

432 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	13	7	20	
Units: percentage of participants				
number (not applicable)	100.0	71.4	90.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at 480 Weeks

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at 480 Weeks

End point description:

This is the percentage of participants with HIV-1 RNA < 50 copies/mL after 480 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

480 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	9	2	11	
Units: percentage of participants				
number (not applicable)	77.8	50.0	72.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at 528 Weeks

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at 528 Weeks

End point description:

This is the percentage of participants with HIV-1 RNA < 50 copies/mL after 528 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

528 weeks

End point values	Tenofovir DF	All TDF		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	6	6		
Units: percentage of participants				
number (not applicable)	100.0	100.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Percentage at 48 Weeks

End point title	Change From Baseline in CD4 Percentage at 48 Weeks

End point description:

This is the change from baseline in CD4 percentage after 48 weeks of exposure to randomized study drug. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

Baseline and 48 weeks

End point values	Tenofovir DF	Stavudine or Zidovudine	All TDF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	46	48	86	
Units: percentage				
arithmetic mean (standard deviation)	0.3 (± 4.49)	1.1 (± 4.73)	0.6 (± 3.85)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Percentage at 96 Weeks

End point title	Change From Baseline in CD4 Percentage at 96 Weeks

End point description:

This is the change from baseline in CD4 percentage after 96 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

Baseline and 96 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	37	38	75	
Units: percentage				
arithmetic mean (standard deviation)	1.3 (± 4.08)	-0.1 (± 3.60)	0.6 (± 3.88)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Percentage at 144 Weeks

End point title	Change From Baseline in CD4 Percentage at 144 Weeks

End point description:

This is the change from baseline in CD4 percentage after 144 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

Baseline and 144 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	33	38	71	
Units: percentage				
arithmetic mean (standard deviation)	0.8 (± 5.61)	-0.1 (± 3.83)	0.3 (± 4.73)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Percentage at 192 Weeks

End point title	Change From Baseline in CD4 Percentage at 192 Weeks

End point description:

This is the change from baseline in CD4 percentage after 192 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

Baseline and 192 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	29	37	66	
Units: percentage				
arithmetic mean (standard deviation)	1.1 (± 5.57)	0.6 (± 3.69)	0.8 (± 4.58)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Percentage at 240 Weeks

End point title	Change From Baseline in CD4 Percentage at 240 Weeks

End point description:

This is the change from baseline in CD4 percentage after 240 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

Baseline and 240 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	28	32	60	
Units: percentage				
arithmetic mean (standard deviation)	1.3 (± 5.98)	-0.9 (± 4.13)	0.1 (± 5.16)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Percentage at 288 Weeks

End point title	Change From Baseline in CD4 Percentage at 288 Weeks

End point description:

This is the change from baseline in CD4 percentage after 288 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

Baseline and 288 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	26	26	52	
Units: percentage				
arithmetic mean (standard deviation)	2.0 (± 6.30)	0.5 (± 4.77)	1.3 (± 5.58)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Percentage at 336 Weeks

End point title	Change From Baseline in CD4 Percentage at 336 Weeks

End point description:

This is the change from baseline in CD4 percentage after 336 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

Baseline and 336 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	23	22	45	
Units: percentage				
arithmetic mean (standard deviation)	2.0 (± 7.19)	0.8 (± 4.01)	1.4 (± 5.82)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Percentage at 384 Weeks

End point title	Change From Baseline in CD4 Percentage at 384 Weeks

End point description:

This is the change from baseline in CD4 percentage after 384 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

Baseline and 384 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	19	10	29	
Units: percentage				
arithmetic mean (standard deviation)	0.5 (± 7.80)	1.6 (± 1.90)	0.9 (± 6.37)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Percentage at 432 Weeks

End point title	Change From Baseline in CD4 Percentage at 432 Weeks

End point description:

This is the change from baseline in CD4 percentage after 432 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

Baseline and 432 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	14	7	21	
Units: percentage				
arithmetic mean (standard deviation)	0.3 (± 6.41)	2.9 (± 3.53)	1.1 (± 5.66)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Percentage at 480 Weeks

End point title	Change From Baseline in CD4 Percentage at 480 Weeks

End point description:

This is the change from baseline in CD4 percentage after 480 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

Baseline and 480 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	3	13	
Units: percentage				
arithmetic mean (standard deviation)	2.3 (± 7.15)	5.0 (± 10.00)	2.9 (± 7.51)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Percentage at 528 Weeks

End point title	Change From Baseline in CD4 Percentage at 528 Weeks

End point description:

This is the change from baseline in CD4 percentage after 528 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

Baseline and 528 weeks

End point values	Tenofovir DF	All TDF		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	6	6		
Units: percentage				
arithmetic mean (standard deviation)	4.5 (± 3.89)	4.5 (± 3.89)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Cell Count (Cells/mm^3) at 48 Weeks

End point title	Change From Baseline in CD4 Cell Count (Cells/mm^3) at 48 Weeks

End point description:

This is the change from baseline in CD4 cell count after 48 weeks of exposure to randomized study drug. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

Baseline and 48 weeks

End point values	Tenofovir DF	Stavudine or Zidovudine	All TDF	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	46	48	86	
Units: cells/mm^3				
arithmetic mean (standard deviation)	-97 (± 416.4)	-11 (± 280.2)	2 (± 385.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Cell Count (Cells/mm^3) at 96 Weeks

End point title	Change From Baseline in CD4 Cell Count (Cells/mm^3) at 96 Weeks

End point description:

This is the change from baseline in CD4 cell count after 96 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

Baseline and 96 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	37	37	74	
Units: cells/mm^3				
arithmetic mean (standard deviation)	-77 (± 408.3)	-56 (± 305.6)	-67 (± 358.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Cell Count (Cells/mm^3) at 144 Weeks

End point title	Change From Baseline in CD4 Cell Count (Cells/mm^3) at 144 Weeks

End point description:

This is the change from baseline in CD4 cell count after 144 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

Baseline and 144 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	33	38	71	
Units: cells/mm^3				
arithmetic mean (standard deviation)	-139 (± 438.2)	-146 (± 245.3)	-142 (± 345.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Cell Count (Cells/mm^3) at 192 Weeks

End point title	Change From Baseline in CD4 Cell Count (Cells/mm^3) at 192 Weeks

End point description:

This is the change from baseline in CD4 cell count after 192 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

Baseline and 192 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	29	37	66	
Units: cells/mm^3				
arithmetic mean (standard deviation)	-304 (± 529.0)	-177 (± 288.5)	-233 (± 413.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Cell Count (Cells/mm^3) at 240 Weeks

End point title	Change From Baseline in CD4 Cell Count (Cells/mm^3) at 240 Weeks

End point description:

This is the change from baseline in CD4 cell count after 240 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

Baseline and 240 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	27	32	59	
Units: cells/mm^3				
arithmetic mean (standard deviation)	-369 (± 529.9)	-296 (± 252.6)	-329 (± 401.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Cell Count (Cells/mm^3) at 288 Weeks

End point title	Change From Baseline in CD4 Cell Count (Cells/mm^3) at 288 Weeks

End point description:

This is the change from baseline in CD4 cell count after 288 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

Baseline and 288 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	26	25	51	
Units: cells/mm^3				
arithmetic mean (standard deviation)	-346 (± 507.5)	-256 (± 292.5)	-302 (± 414.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Cell Count (Cells/mm^3) at 336 Weeks

End point title	Change From Baseline in CD4 Cell Count (Cells/mm^3) at 336 Weeks

End point description:

This is the change from baseline in CD4 cell count after 336 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

Baseline and 336 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	23	22	45	
Units: cells/mm^3				
arithmetic mean (standard deviation)	-415 (± 569.4)	-283 (± 252.2)	-350 (± 443.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Cell Count (Cells/mm^3) at 384 Weeks

End point title	Change From Baseline in CD4 Cell Count (Cells/mm^3) at 384 Weeks

End point description:

This is the change from baseline in CD4 cell count after 384 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded

End point type	Secondary

End point timeframe:

Baseline and 384 weeks

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	19	10	29	
Units: cells/mm^3				
arithmetic mean (standard deviation)	-620 (± 635.6)	-305 (± 238.2)	-512 (± 548.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Cell Count (Cells/mm^3) at 432 Weeks

End point title	Change From Baseline in CD4 Cell Count (Cells/mm^3) at 432 Weeks

End point description:

This is the change from baseline in CD4 cell count after 432 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded

End point type	Secondary
End point timeframe: Baseline and 432 weeks	

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	14	7	21	
Units: cells/mm^3				
arithmetic mean (standard deviation)	-795 (± 559.2)	-302 (± 355.2)	-631 (± 545.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Cell Count (Cells/mm^3) at 480 Weeks

End point title	Change From Baseline in CD4 Cell Count (Cells/mm^3) at 480 Weeks
End point description: This is the change from baseline in CD4 cell count after 480 weeks of exposure to TDF. Intent-to-treat, Missing = Excluded	
End point type	Secondary
End point timeframe: Baseline and 480 weeks	

End point values	Tenofovir DF	(Stavudine or Zidovudine)/TDF	All TDF	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	3	13	
Units: cells/mm^3				
arithmetic mean (standard deviation)	-923 (± 755.4)	-448 (± 469.9)	-813 (± 712.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Cell Count (Cells/mm^3) at 528 Weeks

End point title	Change From Baseline in CD4 Cell Count (Cells/mm^3) at 528 Weeks

End point description:

This is the change from baseline in CD4 cell count after 528 weeks of exposure to TDF. Intent-to-treat,

Missing = Excluded

End point type	Secondary

End point timeframe:

Baseline and 528 weeks

End point values	Tenofovir DF	All TDF		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	6	6		
Units: cells/mm^3				
arithmetic mean (standard deviation)	-710 (± 447.0)	-710 (± 447.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Virologic Success at 48 Weeks (HIV-1 RNA Cutoff at 50 Copies/mL, Snapshot)

End point title	Virologic Success at 48 Weeks (HIV-1 RNA Cutoff at 50 Copies/mL, Snapshot)

End point description:

This is the percentage of participants with virologic success after 48 weeks of exposure to randomized study drug. Participants from the Intent-to-Treat (ITT) Analysis Set who were less than 12 years of age at baseline were analyzed.
The percentage of participants achieving HIV-1 RNA < 50 copies/mL at Week 48 was analyzed using the snapshot algorithm, which defines a patient's virologic response status using only the viral load at the predefined time point within an allowed window of time, along with study drug discontinuation status.

End point type	Secondary

End point timeframe:

48 weeks

End point values	Tenofovir DF	Stavudine or Zidovudine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	48		
Units: percentage of participants				
number (not applicable)	75.0	81.3		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were reported in the open-label randomized period (Weeks 0-48), and during the extension period when all participants received tenofovir DF.

Adverse event reporting additional description:

Tenofovir DF and Stavudine or Zidovudine groups: AEs were reported from baseline through last dose (up to Week 48) + 30 days. AEs with onset during the extension period were excluded;
All TDF group: AEs were reported from baseline through last dose + 30 days (median duration of exposure = 330.7 weeks)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Tenofovir DF

Reporting group description:

Participants in this group received TDF during the randomized phase (48 weeks).

Reporting group title	Stavudine or Zidovudine

Reporting group description:

Participants in this group received stavudine or zidovudine during the randomized phase (48 weeks).

Reporting group title	All TDF

Reporting group description:

All participants who received tenofovir DF in the randomized and/or extension phases

Serious adverse events	Tenofovir DF	Stavudine or Zidovudine	All TDF
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 48 (4.17%)	2 / 49 (4.08%)	15 / 89 (16.85%)
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)			
Brain neoplasm			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 89 (1.12%)
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			
Joint dislocation			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Snake bite			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	2 / 89 (2.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 49 (2.04%)	0 / 89 (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
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 89 (1.12%)
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, thoracic and mediastinal disorders			
Asthmatic crisis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 49 (2.04%)	0 / 89 (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
Musculoskeletal and connective tissue disorders			
Haemarthrosis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Pneumonia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 49 (0.00%)	2 / 89 (2.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngotonsillitis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 49 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amoebiasis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 89 (1.12%)
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 / 48 (0.00%)	0 / 49 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear infection			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymph node abscess			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shigella infection			

subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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	Stavudine or Zidovudine	All TDF
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 48 (77.08%)	35 / 49 (71.43%)	82 / 89 (92.13%)
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 48 (2.08%)	0 / 49 (0.00%)	14 / 89 (15.73%)
occurrences (all)	1	0	16
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	8 / 89 (8.99%)
occurrences (all)	0	0	11
Anaemia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	6 / 89 (6.74%)
occurrences (all)	0	0	7
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 48 (2.08%)	3 / 49 (6.12%)	14 / 89 (15.73%)
occurrences (all)	1	4	25
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	4 / 48 (8.33%)	1 / 49 (2.04%)	20 / 89 (22.47%)
occurrences (all)	5	1	28
Dental caries			
subjects affected / exposed	1 / 48 (2.08%)	1 / 49 (2.04%)	22 / 89 (24.72%)
occurrences (all)	1	1	26
Vomiting			
subjects affected / exposed	6 / 48 (12.50%)	0 / 49 (0.00%)	11 / 89 (12.36%)
occurrences (all)	6	0	15
Gastritis			
subjects affected / exposed	2 / 48 (4.17%)	1 / 49 (2.04%)	8 / 89 (8.99%)
occurrences (all)	2	1	8
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 48 (12.50%)	7 / 49 (14.29%)	20 / 89 (22.47%)
occurrences (all)	7	8	35
Rhinitis allergic			
subjects affected / exposed	4 / 48 (8.33%)	0 / 49 (0.00%)	12 / 89 (13.48%)
occurrences (all)	4	0	19
Nasal congestion			
subjects affected / exposed	0 / 48 (0.00%)	2 / 49 (4.08%)	8 / 89 (8.99%)
occurrences (all)	0	2	10
Asthmatic crisis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 49 (2.04%)	5 / 89 (5.62%)
occurrences (all)	0	1	15
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	8 / 89 (8.99%)
occurrences (all)	0	0	8
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	1 / 48 (2.08%)	1 / 49 (2.04%)	5 / 89 (5.62%)
occurrences (all)	1	1	8
Musculoskeletal and connective tissue disorders			
Arthralgia			

subjects affected / exposed	0 / 48 (0.00%)	1 / 49 (2.04%)	15 / 89 (16.85%)
occurrences (all)	0	1	23
Myalgia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	6 / 89 (6.74%)
occurrences (all)	0	0	7
Infections and infestations			
Viral upper respiratory tract infection			
subjects affected / exposed	17 / 48 (35.42%)	17 / 49 (34.69%)	57 / 89 (64.04%)
occurrences (all)	28	25	221
Otitis media			
subjects affected / exposed	7 / 48 (14.58%)	4 / 49 (8.16%)	16 / 89 (17.98%)
occurrences (all)	9	5	36
Gastroenteritis			
subjects affected / exposed	3 / 48 (6.25%)	4 / 49 (8.16%)	18 / 89 (20.22%)
occurrences (all)	3	4	21
Upper respiratory tract infection			
subjects affected / exposed	6 / 48 (12.50%)	4 / 49 (8.16%)	10 / 89 (11.24%)
occurrences (all)	6	5	25
Pharyngitis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 49 (0.00%)	16 / 89 (17.98%)
occurrences (all)	1	0	21
Pharyngotonsillitis			
subjects affected / exposed	1 / 48 (2.08%)	1 / 49 (2.04%)	14 / 89 (15.73%)
occurrences (all)	1	1	16
Impetigo			
subjects affected / exposed	0 / 48 (0.00%)	2 / 49 (4.08%)	10 / 89 (11.24%)
occurrences (all)	0	3	14
Oral herpes			
subjects affected / exposed	2 / 48 (4.17%)	1 / 49 (2.04%)	9 / 89 (10.11%)
occurrences (all)	2	1	18
Varicella			
subjects affected / exposed	0 / 48 (0.00%)	1 / 49 (2.04%)	10 / 89 (11.24%)
occurrences (all)	0	1	10
Tinea versicolour			
subjects affected / exposed	1 / 48 (2.08%)	1 / 49 (2.04%)	8 / 89 (8.99%)
occurrences (all)	1	1	10

Bronchitis			
subjects affected / exposed	2 / 48 (4.17%)	1 / 49 (2.04%)	6 / 89 (6.74%)
occurrences (all)	2	1	6
Conjunctivitis			
subjects affected / exposed	2 / 48 (4.17%)	0 / 49 (0.00%)	7 / 89 (7.87%)
occurrences (all)	2	0	7
Sinusitis			
subjects affected / exposed	3 / 48 (6.25%)	1 / 49 (2.04%)	5 / 89 (5.62%)
occurrences (all)	4	1	8
Acarodermatitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	8 / 89 (8.99%)
occurrences (all)	0	0	8
Abscess limb			
subjects affected / exposed	1 / 48 (2.08%)	1 / 49 (2.04%)	5 / 89 (5.62%)
occurrences (all)	1	1	6
Fungal skin infection			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	6 / 89 (6.74%)
occurrences (all)	0	0	8
Lice infestation			
subjects affected / exposed	0 / 48 (0.00%)	1 / 49 (2.04%)	5 / 89 (5.62%)
occurrences (all)	0	1	7

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 August 2006	— The planned number of study centers was increased from 1 in Panama to up to 10 in the US and Panama. — The planned number of subjects was increased from 60 (30 per treatment group) to 100 (50 per treatment group). — Administrative clarifications to the protocol were made regarding dispensing of study medication to subjects and requirements for study entry.
14 June 2007	— The study was extended for an additional 2 years. After completing 48 weeks of treatment with study drug or stavudine or zidovudine, eligible subjects from both study groups were given the option to continue (or initiate) tenofovir DF by rolling over into a 96-week study extension. — The study was expanded into the UK.
07 August 2009	— The study was extended for an additional 2 years. After completing the first 96-week study extension with open-label tenofovir DF, currently enrolled subjects at all active sites who have not yet reached 18 years of age (only applicable where tenofovir DF is commercially available for the treatment of HIV-1 infection in adults) and who have shown benefit from tenofovir DF will be given the option to continue receiving tenofovir DF for an additional 96 weeks, or until tenofovir DF becomes commercially available in the country in which the subjects are enrolled, whichever occurs first.
13 May 2011	— The study was extended to include a third 96-week open-label extension for a total of up to 336 weeks. — The interval for DXA scans was increased from every 24 weeks to every 48 weeks after Week 240.
23 January 2012	— Reduced-strength TDF tablets (150, 200, and 250 mg) were added. — A Week 4 visit was added after the switch from TDF powder to TDF tablets. — The US Food and Drug Administration (FDA) snapshot algorithm was added as a secondary efficacy endpoint.
13 February 2013	— A long term extension period was introduced (ie, beyond Week 336).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported