Clinical trial results:
A Phase 2/3, Open-Label, Multi-Cohort Switch Study to Evaluate Emtricitabine/Tenofovir Alafenamide (F/TAF) in HIV-1 Infected Children and Adolescents Virologically Suppressed on a 2-NRTI-Containing Regimen

Summary

EudraCT number	2015-001339-19
Trial protocol	Outside EU/EEA GB
Global end of trial date	

Results information

Result version number	v1 (current)
This version publication date	14 August 2021
First version publication date	14 August 2021

Trial information

Trial identification

Sponsor protocol code	GS-US-311-1269

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02285114
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	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com
Scientific contact	Gilead Clinical Study Information Center, Gilead Sciences, 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-001577-PIP02-14
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	13 December 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 November 2019
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to confirm the tenofovir alafenamide (TAF) dose and to evaluate the pharmacokinetics (PK) of TAF, safety, and tolerability of emtricitabine/tenofovir alafenamide (F/TAF) in human immunodeficiency virus-1 (HIV-1) infected children and adolescents virologically suppressed (defined as having < 50 copies/mL of HIV-1 ribonucleic acid [RNA] for a period of at least 6 months) while on a stable nucleoside reverse transcriptase inhibitor (NRTI) containing regimen.

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:

A 3rd antiretroviral (ARV) agent of the participant's pre-existing regimen may include one of the following: boosted atazanavir (ATV), boosted lopinavir (LPV), boosted darunavir (DRV), unboosted efavirenz (EFV), unboosted nevirapine (NVP), unboosted raltegravir (RAL), or unboosted dolutegravir (DTG).
Boosted protease inhibitors (PIs) of the participant's pre-existing regimen may include one of the following: ATV, LPV, or DRV.

Evidence for comparator: -

Actual start date of recruitment	20 January 2015
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	Panama: 19
Country: Number of subjects enrolled	United States: 10
Country: Number of subjects enrolled	South Africa: 12
Worldwide total number of subjects	41
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)	12
Adolescents (12-17 years)	29
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 Panama, South Africa, and United States. The first participant was screened on 20 January 2015. Participants will not be enrolled in Cohort 2 (Group 1 and 2 in Part B), Cohorts 3 and 4 (Parts A and B).

Pre-assignment

Screening details:

The last Week 48 study visit for participants in Cohort 1 and 2, Group 1 and 2 in Part A occurred on 13 December 2019. It was prespecified to analyze data from Cohort 1 together because both treatments (F/TAF 200/10 mg with boosted 3rd ARV and F/TAF 200/25 mg with unboosted 3rd ARV) were expected to have a similar effect on the efficacy and safety.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	F/TAF+3rd ARV Agent (Cohort 1)

Arm description:

Participants between 12 to < 18 years of age and ≥ 35 kg body weight received F/TAF 200/10 mg fixed-dose combination (FDC) tablet (with boosted 3rd ARV agent) or F/TAF 200/25 mg FDC tablet (with unboosted 3rd ARV agent) orally once daily for 48 weeks. After completion of 48 weeks, all participants will be given the option to participate in an extension phase of the study. Gilead will provide F/TAF until a) the participant turns 18 and F/TAF is commercially available for use in adults in the country in which the participant is enrolled or, b) F/TAF becomes commercially available for pediatric use in the country in which the participant is enrolled or, c) Gilead Sciences elects to terminate development of F/TAF in the applicable country. (Allowed boosted 3rd ARV agents: LPV, ATV, DRV; Allowed unboosted 3rd ARV agents: EFV, RAL, DTG, or NVP)

Arm type	Experimental
Investigational medicinal product name	F/TAF
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200/25 mg for unboosted 3rd agent and 200/10 mg for boosted 3rd agent, administered orally once daily

Arm title	F/TAF+3rd ARV Agent (Cohort 2, Group 1, Part A)

Arm description:

Participants between 6 to < 12 years of age and ≥ 25 kg body weight received F/TAF 200/25 mg FDC tablet orally once daily while continuing on their boosted PI for 48 weeks. After completion of 48 weeks, all participants will be given the option to participate in an extension phase of the study. Gilead will provide F/TAF until a) the participant turns 18 and F/TAF is commercially available for use in adults in the country in which the participant is enrolled or, b) F/TAF becomes commercially available for pediatric use in the country in which the participant is enrolled or, c) Gilead Sciences elects to terminate development of F/TAF in the applicable country. (Allowed boosted PIs: ATV, LPV or DRV)

Arm type	Experimental

Investigational medicinal product name	F/TAF
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200/25 mg administered orally once daily

Arm title	F/TAF+3rd ARV Agent (Cohort 2, Group 2, Part A)

Arm description:

Participants between 2 to < 12 years of age and 17 to < 25 kg body weight received F/TAF 120/15 mg FDC orally once daily while continuing on their 3rd ARV agent for 48 weeks. After completion of 48 weeks, all participants will be given the option to participate in an extension phase of the study. Gilead will provide F/TAF until a) the participant turns 18 and F/TAF is commercially available for use in adults in the country in which the participant is enrolled or, b) F/TAF becomes commercially available for pediatric use in the country in which the participant is enrolled or, c) Gilead Sciences elects to terminate development of F/TAF in the applicable country. (Allowed boosted 3rd ARV agents: LPV, ATV, DRV; Allowed unboosted 3rd ARV agents: EFV, RAL, DTG, or NVP)

Arm type	Experimental
Investigational medicinal product name	F/TAF
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

120/15 mg administered orally once daily

Number of subjects in period 1[1]	F/TAF+3rd ARV Agent (Cohort 1)	F/TAF+3rd ARV Agent (Cohort 2, Group 1, Part A)	F/TAF+3rd ARV Agent (Cohort 2, Group 2, Part A)
Started	28	9	3
Completed	7	2	0
Not completed	21	7	3
Still on study	21	5	2
Withdrew Consent	-	-	1
Investigator's Discretion	-	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: 1 participant who was enrolled in Cohort 1 was not treated and was not included in the Safety Analysis Set for Period 1 table reported above.

Baseline characteristics

Reporting groups	
Reporting group title	F/TAF+3rd ARV Agent (Cohort 1)
Reporting group description:	
Participants between 12 to < 18 years of age and ≥ 35 kg body weight received F/TAF 200/10 mg fixed-dose combination (FDC) tablet (with boosted 3rd ARV agent) or F/TAF 200/25 mg FDC tablet (with unboosted 3rd ARV agent) orally once daily for 48 weeks. After completion of 48 weeks, all participants will be given the option to participate in an extension phase of the study. Gilead will provide F/TAF until a) the participant turns 18 and F/TAF is commercially available for use in adults in the country in which the participant is enrolled or, b) F/TAF becomes commercially available for pediatric use in the country in which the participant is enrolled or, c) Gilead Sciences elects to terminate development of F/TAF in the applicable country. (Allowed boosted 3rd ARV agents: LPV, ATV, DRV; Allowed unboosted 3rd ARV agents: EFV, RAL, DTG, or NVP)	
Reporting group title	F/TAF+3rd ARV Agent (Cohort 2, Group 1, Part A)
Reporting group description:	
Participants between 6 to < 12 years of age and ≥ 25 kg body weight received F/TAF 200/25 mg FDC tablet orally once daily while continuing on their boosted PI for 48 weeks. After completion of 48 weeks, all participants will be given the option to participate in an extension phase of the study. Gilead will provide F/TAF until a) the participant turns 18 and F/TAF is commercially available for use in adults in the country in which the participant is enrolled or, b) F/TAF becomes commercially available for pediatric use in the country in which the participant is enrolled or, c) Gilead Sciences elects to terminate development of F/TAF in the applicable country. (Allowed boosted PIs: ATV, LPV or DRV)	
Reporting group title	F/TAF+3rd ARV Agent (Cohort 2, Group 2, Part A)
Reporting group description:	
Participants between 2 to < 12 years of age and 17 to < 25 kg body weight received F/TAF 120/15 mg FDC orally once daily while continuing on their 3rd ARV agent for 48 weeks. After completion of 48 weeks, all participants will be given the option to participate in an extension phase of the study. Gilead will provide F/TAF until a) the participant turns 18 and F/TAF is commercially available for use in adults in the country in which the participant is enrolled or, b) F/TAF becomes commercially available for pediatric use in the country in which the participant is enrolled or, c) Gilead Sciences elects to terminate development of F/TAF in the applicable country. (Allowed boosted 3rd ARV agents: LPV, ATV, DRV; Allowed unboosted 3rd ARV agents: EFV, RAL, DTG, or NVP)	

Reporting group values	F/TAF+3rd ARV Agent (Cohort 1)	F/TAF+3rd ARV Agent (Cohort 2, Group 1, Part A)	F/TAF+3rd ARV Agent (Cohort 2, Group 2, Part A)
Number of subjects	28	9	3
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	14	10	7
standard deviation	± 1.6	± 1.0	± 1.2
Gender categorical Units: Subjects			
Female	12	5	2
Male	16	4	1
Ethnicity Units: Subjects			
Hispanic or Latino	14	5	1
Not Hispanic or Latino	14	4	2
Race Units: Subjects			

Asian	1	0	0
Black	12	4	2
White	3	0	0
Other	12	5	1
Human Immunodeficiency Virus, Type 1 Ribonucleic Acid (HIV-1 RNA) Units: Subjects			
< 50 copies/mL	27	9	3
≥ 50 copies/mL	1	0	0
Cluster of Differentiation 4 (CD4) Cell Count Units: cells/µL			
arithmetic mean	909	871	1209
standard deviation	± 242.7	± 364.8	± 306.3
CD4 Percentage (%) Units: Percentage of lymphocytes			
arithmetic mean	36.1	36.7	36.1
standard deviation	± 6.40	± 4.35	± 3.35

Reporting group values	Total		
Number of subjects	40		
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	19		
Male	21		
Ethnicity Units: Subjects			
Hispanic or Latino	20		
Not Hispanic or Latino	20		
Race Units: Subjects			
Asian	1		
Black	18		
White	3		
Other	18		
Human Immunodeficiency Virus, Type 1 Ribonucleic Acid (HIV-1 RNA) Units: Subjects			
< 50 copies/mL	39		
≥ 50 copies/mL	1		
Cluster of Differentiation 4 (CD4) Cell Count Units: cells/µL			
arithmetic mean			
standard deviation	-		

CD4 Percentage (%) Units: Percentage of lymphocytes arithmetic mean standard deviation	- 		

End points

End points reporting groups

Reporting group title	F/TAF+3rd ARV Agent (Cohort 1)

Reporting group description:

Participants between 12 to < 18 years of age and ≥ 35 kg body weight received F/TAF 200/10 mg fixed-dose combination (FDC) tablet (with boosted 3rd ARV agent) or F/TAF 200/25 mg FDC tablet (with unboosted 3rd ARV agent) orally once daily for 48 weeks. After completion of 48 weeks, all participants will be given the option to participate in an extension phase of the study. Gilead will provide F/TAF until a) the participant turns 18 and F/TAF is commercially available for use in adults in the country in which the participant is enrolled or, b) F/TAF becomes commercially available for pediatric use in the country in which the participant is enrolled or, c) Gilead Sciences elects to terminate development of F/TAF in the applicable country. (Allowed boosted 3rd ARV agents: LPV, ATV, DRV; Allowed unboosted 3rd ARV agents: EFV, RAL, DTG, or NVP)

Reporting group title	F/TAF+3rd ARV Agent (Cohort 2, Group 1, Part A)

Reporting group description:

Participants between 6 to < 12 years of age and ≥ 25 kg body weight received F/TAF 200/25 mg FDC tablet orally once daily while continuing on their boosted PI for 48 weeks. After completion of 48 weeks, all participants will be given the option to participate in an extension phase of the study. Gilead will provide F/TAF until a) the participant turns 18 and F/TAF is commercially available for use in adults in the country in which the participant is enrolled or, b) F/TAF becomes commercially available for pediatric use in the country in which the participant is enrolled or, c) Gilead Sciences elects to terminate development of F/TAF in the applicable country. (Allowed boosted PIs: ATV, LPV or DRV)

Reporting group title	F/TAF+3rd ARV Agent (Cohort 2, Group 2, Part A)

Reporting group description:

Participants between 2 to < 12 years of age and 17 to < 25 kg body weight received F/TAF 120/15 mg FDC orally once daily while continuing on their 3rd ARV agent for 48 weeks. After completion of 48 weeks, all participants will be given the option to participate in an extension phase of the study. Gilead will provide F/TAF until a) the participant turns 18 and F/TAF is commercially available for use in adults in the country in which the participant is enrolled or, b) F/TAF becomes commercially available for pediatric use in the country in which the participant is enrolled or, c) Gilead Sciences elects to terminate development of F/TAF in the applicable country. (Allowed boosted 3rd ARV agents: LPV, ATV, DRV; Allowed unboosted 3rd ARV agents: EFV, RAL, DTG, or NVP)

Subject analysis set title	F/TAF 200/10 mg+3rd ARV Agent (Cohort 1)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants between 12 to < 18 years of age and ≥ 35 kg body weight received F/TAF 200/10 mg FDC tablet (with boosted 3rd ARV agent) orally once daily for 48 weeks. After completion of 48 weeks, all participants will be given the option to participate in an extension phase of the study. Gilead will provide F/TAF until a) the participant turns 18 and F/TAF is commercially available for use in adults in the country in which the participant is enrolled or, b) F/TAF becomes commercially available for pediatric use in the country in which the participant is enrolled or, c) Gilead Sciences elects to terminate development of F/TAF in the applicable country. (Allowed boosted 3rd ARV agents: LPV, ATV, DRV)

Subject analysis set title	F/TAF 200/25 mg+3rd ARV Agent (Cohort 1)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants between 12 to < 18 years of age and ≥ 35 kg body weight received F/TAF 200/25 mg FDC tablet (with unboosted 3rd ARV agent) orally once daily for 48 weeks. After completion of 48 weeks, all participants will be given the option to participate in an extension phase of the study. Gilead will provide F/TAF until a) the participant turns 18 and F/TAF is commercially available for use in adults in the country in which the participant is enrolled or, b) F/TAF becomes commercially available for pediatric use in the country in which the participant is enrolled or, c) Gilead Sciences elects to terminate development of F/TAF in the applicable country. (Allowed unboosted 3rd ARV agents: EFV, RAL, DTG, or NVP)

Primary: Pharmacokinetic (PK) Parameter (Cohort 1): AUCtau of Tenofovir Alafenamide (TAF)

End point title	Pharmacokinetic (PK) Parameter (Cohort 1): AUCtau of Tenofovir Alafenamide (TAF)[1]

End point description:

AUCtau is defined as concentration of drug over time (the area under the concentration versus time curve over the dosing interval). Participants in the Intensive PK (IPK) Analysis Set (participants who were enrolled in Cohort 1 for IPK evaluation, had received at least one dose of study medication, and had at least 1 non-missing PK concentration data for any analyte of interest [e.g., emtricitabine {FTC}, TAF, and tenofovir {TFV}]) with available data were analyzed.

End point type	Primary

End point timeframe:

Any time at Week 2 visit

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical comparison was planned or performed.

End point values	F/TAF 200/10 mg+3rd ARV Agent (Cohort 1)	F/TAF 200/25 mg+3rd ARV Agent (Cohort 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	9	9		
Units: h*ng/mL				
arithmetic mean (standard deviation)	139.9 (± 113.23)	200.6 (± 83.80)		

Statistical analyses

No statistical analyses for this end point

Primary: PK Parameter (Cohort 2): AUCtau of TAF

End point title	PK Parameter (Cohort 2): AUCtau of TAF[2][3]

End point description:

AUCtau is defined as concentration of drug over time (the area under the concentration versus time curve over the dosing interval). The PK Analysis Set included all participants who were enrolled into the study, had received at least one dose of study medication, and had at least 1 non-missing PK concentration data for any analyte of interest (e.g., FTC, TAF, and TFV).

End point type	Primary

End point timeframe:

Any time at Week 2 or Week 4 visit, or within 7 days after the completion of Week 2 or Week 4 visits

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical comparison was planned or performed.

[3] - 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: The end point is reporting statistics for Cohort 2 only.

End point values	F/TAF+3rd ARV Agent (Cohort 2, Group 1, Part A)	F/TAF+3rd ARV Agent (Cohort 2, Group 2, Part A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	3		
Units: h*ng/mL				
arithmetic mean (standard deviation)	210.8 (± 97.35)	220.2 (± 187.96)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Experiencing Treatment-Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs) Through Week 24

End point title	Percentage of Participants Experiencing Treatment-Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs) Through Week 24[4]

End point description:

An AE is any untoward medical occurrence in a clinical study participant which does not necessarily have a causal relationship with the treatment. An AE can therefore be any unfavorable and/or unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. The TEAEs were defined as any AEs with an onset date of on or after the study drug start date and no later than 30 days after permanent discontinuation of study drug or any AEs leading to premature discontinuation of study drug. The Safety Analysis Set included all participants who were enrolled in the study and had received at least one dose of study medication. It was prespecified to analyze data from Cohort 1 together because both treatments (F/TAF 200/10 mg with boosted 3rd ARV and F/TAF 200/25 mg with unboosted 3rd ARV) were expected to have a similar effect on the efficacy and safety for the target population.

End point type	Primary

End point timeframe:

Baseline through Week 24

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical comparison was planned or performed.

End point values	F/TAF+3rd ARV Agent (Cohort 1)	F/TAF+3rd ARV Agent (Cohort 2, Group 1, Part A)	F/TAF+3rd ARV Agent (Cohort 2, Group 2, Part A)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	9	3	
Units: percentage of participants				
number (not applicable)				
Any AEs	82.1	66.7	66.7	
SAEs	7.1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter (Cohort 1): Cmax of TAF, FTC, and TFV

End point title	PK Parameter (Cohort 1): Cmax of TAF, FTC, and TFV

End point description:

Cmax is defined as the maximum concentration of drug. Participants in the IPK Analysis Set with

available data were analyzed.

End point type	Secondary

End point timeframe:

Any time at Week 2 visit

End point values	F/TAF 200/10 mg+3rd ARV Agent (Cohort 1)	F/TAF 200/25 mg+3rd ARV Agent (Cohort 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	11		
Units: ng/mL				
arithmetic mean (standard deviation)				
Cmax of TAF	89.1 (± 77.63)	139.3 (± 76.17)		
Cmax of FTC	2259.2 (± 470.75)	2320.0 (± 482.18)		
Cmax of TFV	21.2 (± 4.89)	11.6 (± 2.74)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter (Cohort 2): Cmax of TAF, FTC, and TFV

End point title	PK Parameter (Cohort 2): Cmax of TAF, FTC, and TFV[5]

End point description:

Cmax is defined as the maximum concentration of drug. Participants in the PK Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Any time at Week 2 or Week 4 visit, or within 7 days after the completion of Week 2 or Week 4 visits

Notes:

[5] - 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: The end point is reporting statistics for Cohort 2 only.

End point values	F/TAF+3rd ARV Agent (Cohort 2, Group 1, Part A)	F/TAF+3rd ARV Agent (Cohort 2, Group 2, Part A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	3		
Units: ng/mL				
arithmetic mean (standard deviation)				
Cmax of TAF	230.4 (± 264.70)	232.0 (± 253.59)		
Cmax of FTC	2074.4 (± 565.91)	2020.0 (± 1151.91)		
Cmax of TFV	55.8 (± 19.20)	48.1 (± 8.07)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter (Cohort 1): Clast of TAF

End point title	PK Parameter (Cohort 1): Clast of TAF

End point description:

Clast is defined as the last observable concentration of drug. Participants in the IPK Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Any time at Week 2 visit

End point values	F/TAF 200/10 mg+3rd ARV Agent (Cohort 1)	F/TAF 200/25 mg+3rd ARV Agent (Cohort 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	11		
Units: ng/mL				
arithmetic mean (standard deviation)	2.2 (± 0.98)	5.5 (± 3.76)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter (Cohort 2) : Clast of TAF

End point title	PK Parameter (Cohort 2) : Clast of TAF[6]

End point description:

Clast is defined as the last observable concentration of drug. Participants in the PK Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Any time at Week 2 or Week 4 visit, or within 7 days after the completion of Week 2 or Week 4 visits

Notes:

[6] - 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: The end point is reporting statistics for Cohort 2 only.

End point values	F/TAF+3rd ARV Agent (Cohort 2, Group 1, Part A)	F/TAF+3rd ARV Agent (Cohort 2, Group 2, Part A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	3		
Units: ng/mL				
arithmetic mean (standard deviation)	2.9 (± 2.32)	2.1 (± 0.86)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter (Cohort 1): CL/F of TAF

End point title	PK Parameter (Cohort 1): CL/F of TAF

End point description:

CL/F is defined as the apparent oral clearance following administration of the drug. Participants in the IPK Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Any time at Week 2 visit

End point values	F/TAF 200/10 mg+3rd ARV Agent (Cohort 1)	F/TAF 200/25 mg+3rd ARV Agent (Cohort 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	9	9		
Units: L/hr				
arithmetic mean (standard deviation)	129.8 (± 101.67)	143.4 (± 53.55)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter (Cohort 2): CL/F of TAF

End point title	PK Parameter (Cohort 2): CL/F of TAF[7]

End point description:

CL/F is defined as the apparent oral clearance following administration of the drug. Participants in the PK Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Any time at Week 2 or Week 4 visit, or within 7 days after the completion of Week 2 or Week 4 visits

Notes:

[7] - 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: The end point is reporting statistics for Cohort 2 only.

End point values	F/TAF+3rd ARV Agent (Cohort 2, Group 1, Part A)	F/TAF+3rd ARV Agent (Cohort 2, Group 2, Part A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	3		
Units: L/hr				
arithmetic mean (standard deviation)	174.3 (± 156.75)	102.1 (± 60.75)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter (Cohort 1): Vz/F of TAF

End point title	PK Parameter (Cohort 1): Vz/F of TAF

End point description:

Vz/F is defined as the apparent volume of distribution of the drug. Participants in the IPK Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Any time at Week 2 visit

End point values	F/TAF 200/10 mg+3rd ARV Agent (Cohort 1)	F/TAF 200/25 mg+3rd ARV Agent (Cohort 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	9	9		
Units: liters				
arithmetic mean (standard deviation)	87.3 (± 60.68)	95.3 (± 43.47)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter (Cohort 2): Vz/F of TAF

End point title	PK Parameter (Cohort 2): Vz/F of TAF[8]

End point description:

Vz/F is defined as the apparent volume of distribution of the drug. Participants in the PK Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Any time at Week 2 or Week 4 visit, or within 7 days after the completion of Week 2 or Week 4 visits

Notes:

[8] - 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: The end point is reporting statistics for Cohort 2 only.

End point values	F/TAF+3rd ARV Agent (Cohort 2, Group 1, Part A)	F/TAF+3rd ARV Agent (Cohort 2, Group 2, Part A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	3		
Units: liters				
arithmetic mean (standard deviation)	160.8 (± 145.57)	63.1 (± 63.39)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter (Cohort 1): AUCtau of FTC and TFV

End point title	PK Parameter (Cohort 1): AUCtau of FTC and TFV

End point description:

AUCtau is defined as concentration of drug over time (the area under the concentration versus time curve over the dosing interval). Participants in the IPK Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Any time at Week 2 visit

End point values	F/TAF 200/10 mg+3rd ARV Agent (Cohort 1)	F/TAF 200/25 mg+3rd ARV Agent (Cohort 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	11		
Units: h*ng/mL				
arithmetic mean (standard deviation)				
AUCtau of FTC	14769.9 (± 4481.23)	14339.8 (± 6099.55)		
AUCtau of TFV	415.5 (± 105.92)	193.2 (± 46.73)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter (Cohort 2): AUCtau of FTC and TFV

End point title	PK Parameter (Cohort 2): AUCtau of FTC and TFV[9]

End point description:

AUCtau is defined as concentration of drug over time (the area under the concentration versus time curve over the dosing interval). Participants in the PK Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Any time at Week 2 or Week 4 visit, or within 7 days after the completion of Week 2 or Week 4 visits

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: The end point is reporting statistics for Cohort 2 only.

End point values	F/TAF+3rd ARV Agent (Cohort 2, Group 1, Part A)	F/TAF+3rd ARV Agent (Cohort 2, Group 2, Part A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	3		
Units: h*ng/mL				
arithmetic mean (standard deviation)				
AUCtau of FTC (N = 8, 3)	12360.8 (± 2928.36)	11171.7 (± 2921.64)		
AUCtau of TFV (N = 9, 3)	999.4 (± 409.33)	908.2 (± 90.62)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter (Cohort 1): Ctau of FTC and TFV

End point title	PK Parameter (Cohort 1): Ctau of FTC and TFV

End point description:

Ctau is defined as the observed drug concentration at the end of the dosing interval. Participants in the IPK Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Any time at Week 2 visit

End point values	F/TAF 200/10 mg+3rd ARV Agent (Cohort 1)	F/TAF 200/25 mg+3rd ARV Agent (Cohort 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	11		
Units: ng/mL				
arithmetic mean (standard deviation)				
Ctau of FTC	223.4 (± 482.59)	301.7 (± 624.77)		
Ctau of TFV	15.7 (± 4.11)	6.7 (± 3.00)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter (Cohort 2): Ctau of FTC and TFV

End point title	PK Parameter (Cohort 2): Ctau of FTC and TFV[10]

End point description:

Ctau is defined as the observed drug concentration at the end of the dosing interval. Participants in the PK Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Any time at Week 2 or Week 4 visit, or within 7 days after the completion of Week 2 or Week 4 visits

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: The end point is reporting statistics for Cohort 2 only.

End point values	F/TAF+3rd ARV Agent (Cohort 2, Group 1, Part A)	F/TAF+3rd ARV Agent (Cohort 2, Group 2, Part A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	3		
Units: ng/mL				
arithmetic mean (standard deviation)				
Ctau of FTC (N = 8, 3)	75.4 (± 22.71)	75.4 (± 27.63)		
Ctau of TFV (N = 9, 3)	34.8 (± 16.39)	30.9 (± 3.53)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing TEAEs and SAEs Through Week 48

End point title	Percentage of Participants Experiencing TEAEs and SAEs Through Week 48

End point description:

An AE is any untoward medical occurrence in a clinical study participant which does not necessarily have a causal relationship with the treatment. An AE can therefore be any unfavorable and/or unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. The TEAEs were defined as any AEs with an onset date of on or after the study drug start date and no later than 30 days after permanent discontinuation of study drug or any AEs leading to premature discontinuation of study drug. Participants in the Safety Analysis Set were analyzed. It was prespecified to analyze data from Cohort 1 together because both treatments (F/TAF 200/10 mg with boosted 3rd ARV and F/TAF 200/25 mg with unboosted 3rd ARV) were expected to have a similar effect on the efficacy and safety for the target population.

End point type	Secondary

End point timeframe:

Baseline through Week 48

End point values	F/TAF+3rd ARV Agent (Cohort 1)	F/TAF+3rd ARV Agent (Cohort 2, Group 1, Part A)	F/TAF+3rd ARV Agent (Cohort 2, Group 2, Part A)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	9	3	
Units: percentage of participants				
number (not applicable)				
Any AEs	85.7	77.8	66.7	
SAEs	7.1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 24, as Defined by the United States Food and Drug Administration (US FDA)-Defined Snapshot Algorithm

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 24, as Defined by the United States Food and Drug Administration (US FDA)-Defined Snapshot Algorithm

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 24 was analyzed using the snapshot algorithm, which defined a participant'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. The Full Analysis Set included all participants who were enrolled in the study and had received at least one dose of study medication. It was prespecified to analyze data from Cohort 1 together because both treatments (F/TAF 200/10 mg with boosted 3rd ARV and F/TAF 200/25 mg with unboosted 3rd ARV) were expected to have a similar effect on the efficacy and safety for the target population.

End point type	Secondary

End point timeframe:

Week 24

End point values	F/TAF+3rd ARV Agent (Cohort 1)	F/TAF+3rd ARV Agent (Cohort 2, Group 1, Part A)	F/TAF+3rd ARV Agent (Cohort 2, Group 2, Part A)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	9	3	
Units: percentage of participants				
number (not applicable)	92.9	100.0	66.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 48, as Defined by the US FDA-Defined Snapshot Algorithm

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 48, as Defined by the US FDA-Defined Snapshot Algorithm

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 48 was analyzed using the snapshot algorithm, which defined a participant'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. Participants in the Full Analysis Set with available data were analyzed. It was prespecified to analyze data from Cohort 1 together because both treatments (F/TAF 200/10 mg with boosted 3rd ARV and F/TAF 200/25 mg with unboosted 3rd ARV) were expected to have a similar effect on the efficacy and safety for the target population.

End point type	Secondary

End point timeframe:

Week 48

End point values	F/TAF+3rd ARV Agent (Cohort 1)	F/TAF+3rd ARV Agent (Cohort 2, Group 1, Part A)	F/TAF+3rd ARV Agent (Cohort 2, Group 2, Part A)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	9	3	
Units: percentage of participants				
number (not applicable)	89.3	77.8	66.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4+ Cell Count at Week 24

End point title	Change From Baseline in CD4+ Cell Count at Week 24

End point description:

Participants in the Full Analysis Set with available data were analyzed. It was prespecified to analyze data from Cohort 1 together because both treatments (F/TAF 200/10 mg with boosted 3rd ARV and F/TAF 200/25 mg with unboosted 3rd ARV) were expected to have a similar effect on the efficacy and safety for the target population.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	F/TAF+3rd ARV Agent (Cohort 1)	F/TAF+3rd ARV Agent (Cohort 2, Group 1, Part A)	F/TAF+3rd ARV Agent (Cohort 2, Group 2, Part A)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	8	2	
Units: cells/µL				
arithmetic mean (standard deviation)	-130 (± 272.6)	68 (± 352.5)	-299 (± 48.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4+ Cell Count at Week 48

End point title	Change From Baseline in CD4+ Cell Count at Week 48

End point description:

Participants in the Full Analysis Set with available data were analyzed. It was prespecified to analyze data from Cohort 1 together because both treatments (F/TAF 200/10 mg with boosted 3rd ARV and F/TAF 200/25 mg with unboosted 3rd ARV) were expected to have a similar effect on the efficacy and safety for the target population.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	F/TAF+3rd ARV Agent (Cohort 1)	F/TAF+3rd ARV Agent (Cohort 2, Group 1, Part A)	F/TAF+3rd ARV Agent (Cohort 2, Group 2, Part A)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	9	2	
Units: cells/µL				
arithmetic mean (standard deviation)	-105 (± 162.9)	210 (± 406.5)	-124 (± 37.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Percentage at Week 24

End point title	Change From Baseline in CD4 Percentage at Week 24

End point description:

Participants in the Full Analysis Set with available data were analyzed. It was prespecified to analyze data from Cohort 1 together because both treatments (F/TAF 200/10 mg with boosted 3rd ARV and F/TAF 200/25 mg with unboosted 3rd ARV) were expected to have a similar effect on the efficacy and

safety for the target population.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	F/TAF+3rd ARV Agent (Cohort 1)	F/TAF+3rd ARV Agent (Cohort 2, Group 1, Part A)	F/TAF+3rd ARV Agent (Cohort 2, Group 2, Part A)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	8	2	
Units: percentage of lymphocytes				
arithmetic mean (standard deviation)	-0.2 (± 3.84)	1.3 (± 2.40)	0.6 (± 5.80)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Percentage at Week 48

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

End point description:

Participants in the Full Analysis Set with available data were analyzed. It was prespecified to analyze data from Cohort 1 together because both treatments (F/TAF 200/10 mg with boosted 3rd ARV and F/TAF 200/25 mg with unboosted 3rd ARV) were expected to have a similar effect on the efficacy and safety for the target population.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	F/TAF+3rd ARV Agent (Cohort 1)	F/TAF+3rd ARV Agent (Cohort 2, Group 1, Part A)	F/TAF+3rd ARV Agent (Cohort 2, Group 2, Part A)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	7	2	
Units: percentage of lymphocytes				
arithmetic mean (standard deviation)	-0.2 (± 3.41)	0.7 (± 3.52)	3.7 (± 7.28)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Palatability of F/TAF Formulation

End point title	Percentage of Participants With Palatability of F/TAF Formulation

End point description:

Palatability was reported based on the product taste of being normal or abnormal. Missing data were reported separately. Participants in the Safety Analysis Set were analyzed. It was prespecified to analyze data from Cohort 1 together because both treatments (F/TAF 200/10 mg with boosted 3rd ARV and F/TAF 200/25 mg with unboosted 3rd ARV) were expected to have a similar effect on the efficacy and safety for the target population. Here, '99999' signifies data not available since no participants were analyzed at the specified timepoint.

End point type	Secondary

End point timeframe:

Week 2 (for Cohort 1), Week 2 and Week 4 (for Cohort 2)

End point values	F/TAF+3rd ARV Agent (Cohort 1)	F/TAF+3rd ARV Agent (Cohort 2, Group 1, Part A)	F/TAF+3rd ARV Agent (Cohort 2, Group 2, Part A)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	9	3	
Units: percentage of participants				
number (not applicable)				
Week 2: Product Taste Normal (N=28,9,3)	89.3	77.8	66.7	
Week 2: Product Taste Abnormal (N=28,9,3)	0	22.2	0	
Week 2: Missing (N=28,9,3)	10.7	0	33.3	
Week 4: Product Taste Normal (N=0,9,3)	99999	66.7	100.0	
Week 4: Product Taste Abnormal (N=0,9,3)	99999	33.3	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Acceptability of F/TAF Formulation

End point title	Percentage of Participants With Acceptability of F/TAF Formulation

End point description:

Acceptability was reported based on the the product size and shape. Missing data were reported separately. Participants in the Safety Analysis Set were analyzed. It was prespecified to analyze data from Cohort 1 together because both treatments (F/TAF 200/10 mg with boosted 3rd ARV and F/TAF 200/25 mg with unboosted 3rd ARV) were expected to have a similar effect on the efficacy and safety for the target population.

End point type	Secondary

End point timeframe:

Baseline up to Week 4

End point values	F/TAF+3rd ARV Agent (Cohort 1)	F/TAF+3rd ARV Agent (Cohort 2, Group 1, Part A)	F/TAF+3rd ARV Agent (Cohort 2, Group 2, Part A)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	9	3	
Units: percentage of participants				
number (not applicable)				
Acceptable Shape and Size	89.3	100.0	100.0	
Product Shape Issue	0	0	0	
Product Size Issue	0	0	0	
Missing	10.7	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

First dose date up to Week 48

Adverse event reporting additional description:

Safety Analysis Set: all participants who were enrolled in study and had received at least 1 dose of study medication. It was prespecified to analyze data from Cohort 1 together because both treatments (F/TAF 200/10 mg with boosted 3rd ARV and F/TAF 200/25 mg with unboosted 3rd ARV) were expected to have a similar effect on the efficacy and safety.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	F/TAF+3rd ARV Agent (Cohort 1)

Reporting group description:

Participants between 12 to < 18 years of age and ≥ 35 kg body weight received F/TAF 200/10 mg FDC tablet (with boosted 3rd ARV agent) or F/TAF 200/25 mg FDC tablet (with unboosted 3rd ARV agent) orally once daily for 48 weeks. After completion of 48 weeks, all participants will be given the option to participate in an extension phase of the study. Gilead will provide F/TAF until a) the participant turns 18 and F/TAF is commercially available for use in adults in the country in which the participant is enrolled or, b) F/TAF becomes commercially available for pediatric use in the country in which the participant is enrolled or, c) Gilead Sciences elects to terminate development of F/TAF in the applicable country. (Allowed boosted 3rd ARV agents: LPV, ATV, DRV; Allowed unboosted 3rd ARV agents: EFV, RAL, DTG, or NVP)

Reporting group title	F/TAF+3rd ARV Agent (Cohort 2, Group 1, Part A)

Reporting group description:

Participants between 6 to < 12 years of age and ≥ 25 kg body weight received F/TAF 200/25 mg FDC tablet orally once daily while continuing on their boosted PI for 48 weeks. After completion of 48 weeks, all participants will be given the option to participate in an extension phase of the study. Gilead will provide F/TAF until a) the participant turns 18 and F/TAF is commercially available for use in adults in the country in which the participant is enrolled or, b) F/TAF becomes commercially available for pediatric use in the country in which the participant is enrolled or, c) Gilead Sciences elects to terminate development of F/TAF in the applicable country. (Allowed boosted PIs: ATV, LPV or DRV)

Reporting group title	F/TAF+3rd ARV Agent (Cohort 2, Group 2, Part A)

Reporting group description:

Participants between 2 to < 12 years of age and 17 to < 25 kg body weight received F/TAF 120/15 mg FDC orally once daily while continuing on their 3rd ARV agent for 48 weeks. After completion of 48 weeks, all participants will be given the option to participate in an extension phase of the study. Gilead will provide
F/TAF until a) the participant turns 18 and F/TAF is commercially available for use in adults in the country in which the participant is enrolled or, b) F/TAF becomes commercially available for pediatric use in the country in which the participant is enrolled or, c) Gilead Sciences elects to terminate development of F/TAF in the
applicable country. (Allowed boosted 3rd ARV agents: LPV, ATV, DRV; Allowed unboosted 3rd ARV agents: EFV, RAL, DTG, or NVP)

Serious adverse events	F/TAF+3rd ARV Agent (Cohort 1)	F/TAF+3rd ARV Agent (Cohort 2, Group 1, Part A)	F/TAF+3rd ARV Agent (Cohort 2, Group 2, Part A)
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 28 (7.14%)	0 / 9 (0.00%)	0 / 3 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from	0	0	0

adverse events			
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 28 (3.57%)	0 / 9 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 28 (3.57%)	0 / 9 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Electrolyte imbalance			
subjects affected / exposed	1 / 28 (3.57%)	0 / 9 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	F/TAF+3rd ARV Agent (Cohort 1)	F/TAF+3rd ARV Agent (Cohort 2, Group 1, Part A)	F/TAF+3rd ARV Agent (Cohort 2, Group 2, Part A)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 28 (75.00%)	7 / 9 (77.78%)	2 / 3 (66.67%)
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 28 (0.00%)	1 / 9 (11.11%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Skin laceration			
subjects affected / exposed	0 / 28 (0.00%)	0 / 9 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 28 (25.00%)	0 / 9 (0.00%)	0 / 3 (0.00%)
occurrences (all)	7	0	0
Dizziness			

subjects affected / exposed	2 / 28 (7.14%)	0 / 9 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 9 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Eye disorders			
Vernal keratoconjunctivitis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 9 (11.11%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	5 / 28 (17.86%)	0 / 9 (0.00%)	0 / 3 (0.00%)
occurrences (all)	6	0	0
Diarrhoea			
subjects affected / exposed	3 / 28 (10.71%)	0 / 9 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Dental caries			
subjects affected / exposed	0 / 28 (0.00%)	2 / 9 (22.22%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Nausea			
subjects affected / exposed	2 / 28 (7.14%)	0 / 9 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 9 (11.11%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Rhinitis allergic			
subjects affected / exposed	3 / 28 (10.71%)	0 / 9 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Nasal congestion			
subjects affected / exposed	2 / 28 (7.14%)	0 / 9 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Skin and subcutaneous tissue disorders			

Acne			
subjects affected / exposed	2 / 28 (7.14%)	0 / 9 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Dermatitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 9 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 28 (14.29%)	3 / 9 (33.33%)	0 / 3 (0.00%)
occurrences (all)	5	6	0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 28 (3.57%)	0 / 9 (0.00%)	2 / 3 (66.67%)
occurrences (all)	1	0	3
Hordeolum			
subjects affected / exposed	2 / 28 (7.14%)	0 / 9 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Influenza			
subjects affected / exposed	2 / 28 (7.14%)	0 / 9 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Pharyngitis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 9 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	3
Upper respiratory tract infection			
subjects affected / exposed	2 / 28 (7.14%)	0 / 9 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Gastroenteritis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 9 (11.11%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Otitis externa			
subjects affected / exposed	0 / 28 (0.00%)	1 / 9 (11.11%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	4 / 28 (14.29%)	0 / 9 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 November 2014	- Study design has been updated from "tenofovir disoproxil fumarate (TDF)-containing regimen" to "2-NRTI-containing regimen" as stable TDF use prior to study entry is no longer a requirement. - There is no longer a requirement to stratify participants by 3rd ARV agents. - Participants are now allowed to use ATV/r and DVR/r as 3rd ARV. - Information regarding recommended F/TAF and FTC/TDF doses for Cohort 2 has been included. - Timing of assessments specific to Cohort 2 is included.
02 August 2017	- F/TAF was approved in the US and EU for use in adolescents based on Genvoya data, which provides support for opening Cohorts 2 enrollment and adding Cohorts 3 and 4. Dose, statistical methods and study procedures have been amended as appropriate. - FTC/TDF reference therapy has been removed from Cohort 2 since F/TAF has been approved for use in adolescents. Participants will no longer be randomized 2:1 ratio into F/TAF and FTC/TDF. Instead, all participants enrolled into Cohorts 2, 3 and 4 will receive F/TAF. - Treatment Assessment period has been changed from 96 weeks to 48 weeks since FTC/TDF reference therapy has been removed from Cohort 2. Study procedures have been updated to reflect the change. Gilead was interested in long-term (96-week) evaluation of TDF on bone and renal parameters during the initial design of this study due to associations between TDF and early-onset bone demineralization in adults and nephrotoxicity, and because the renal and bone safety of TAF had not yet been established. However, since the initiation of Study GS-US-311-1269, recent studies have demonstrated that renal and bone effects were significantly reduced in participants receiving TAF- versus TDF-containing regimens. As such, randomization to TDF is not deemed pertinent to the clinical development of pediatric DVY and has been removed as the reference therapy from Study GS-US-311-1269. The elimination of the TDF reference therapy arm in the study thus allows for a shortened treatment duration of 48 weeks.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported