



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 | 11 December 2024 |

Results information

| | |
|--------------------------------|-----------------------------------------------------------------------------------------------------------------------------------|
| Result version number | v2 (current) |
| This version publication date | 25 June 2025 |
| First version publication date | 14 August 2021 |
| Version creation reason | <ul style="list-style-type: none">New data added to full data set The record is revised to add final analysis data. |

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) | EMA-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 | Final |
| Date of interim/final analysis | 11 December 2024 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 11 December 2024 |
| Was the trial ended prematurely? | 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 2 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 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).

Evidence for comparator: -

| | |
|-----------------------------------------------------------|-----------------|
| Actual start date of recruitment | 20 January 2015 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Panama: 19 |
| Country: Number of subjects enrolled | South Africa: 12 |
| Country: Number of subjects enrolled | United States: 10 |
| 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:

49 participants were screened. Participants were enrolled at study sites in Panama, South Africa, and United States. The study had a main treatment phase of 48 weeks and an extension phase.

Pre-assignment

Screening details:

No participant was enrolled in Cohort 2 (Part B: Groups 1 and 2), and Cohorts 3 and 4 (Parts A and B). Data is reported only for Cohorts 1 and 2 (Part A: Groups 1 and 2). It was prespecified to analyze Cohort 1 together as both treatments were expected to have a similar effect on efficacy and safety for target population.

Period 1

| | |
|------------------------------|----------------|
| Period 1 title | Main Phase |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

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

Arm description:

Participants between 12 to < 18 years of age and ≥ 35 kg body weight received emtricitabine/tenofovir alafenamide (F/TAF) 200/10 mg fixed-dose combination (FDC) tablet (with boosted 3rd antiretroviral [ARV] agent) or F/TAF 200/25 mg FDC tablet (with unboosted 3rd ARV agent) orally once daily for 48 weeks. 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 | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 1) |
|------------------|--------------------------------------------------------------|

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 protease inhibitor (PI) for 48 weeks. 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 | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 2) |
|------------------|--------------------------------------------------------------|

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. 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] | Main Phase: F/TAF+3rd ARV Agent (Cohort 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 2) |
|-----------------------------------------------|--------------------------------------------|--------------------------------------------------------------|--------------------------------------------------------------|
| | | | |
| Started | 28 | 9 | 3 |
| Completed | 28 | 7 | 2 |
| Not completed | 0 | 2 | 1 |
| 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 but not treated was not included in the Safety Analysis Set for Period 1 table reported above.

Period 2

| | |
|------------------------------|-----------------|
| Period 2 title | Extension Phase |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

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

Arm description:

After completion of 48 weeks, all participants were given the option to participate in an extension phase of the study to continue with F/TAF+3rd ARV agent. Gilead provided F/TAF until a) the participant turned 18 and F/TAF was commercially available for use in adults in the country in which the participant was enrolled or, b) F/TAF became commercially available for pediatric use in the country in which the participant was enrolled or, c) Gilead Sciences elected to terminate development of F/TAF in the applicable country. The maximum exposure was 438.9 weeks. 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 | Extension Phase:F/TAF+3rd ARV Agent (Cohort 2, Part A-Group 1) |
|------------------|----------------------------------------------------------------|

Arm description:

After completion of 48 weeks, all participants were given the option to participate in an extension phase of the study to continue with F/TAF+3rd ARV agent. Gilead provided F/TAF until a) the participant turned 18 and F/TAF was commercially available for use in adults in the country in which the participant was enrolled or, b) F/TAF became commercially available for pediatric use in the country in which the participant is enrolled or, c) Gilead Sciences elected to terminate development of F/TAF in the applicable country. The maximum exposure was 315.0 weeks. 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 | Extension Phase:F/TAF+3rd ARV Agent (Cohort 2, Part A-Group 2) |
|------------------|----------------------------------------------------------------|

Arm description:

After completion of 48 weeks, all participants were given the option to participate in an extension phase of the study to continue with F/TAF+3rd ARV Agent. Gilead provided F/TAF until a) the participant turned 18 and F/TAF was commercially available for use in adults in the country in which the participant was enrolled or, b) F/TAF became commercially available for pediatric use in the country in which the participant was enrolled or, c) Gilead Sciences elected to terminate development of F/TAF in the applicable country. The maximum exposure was 103.1 weeks. 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 2 | Extension Phase: F/TAF+3rd ARV Agent (Cohort 1) | Extension Phase:F/TAF+3rd ARV Agent (Cohort 2, Part A-Group 1) | Extension Phase:F/TAF+3rd ARV Agent (Cohort 2, Part A-Group 2) |
|--------------------------------|-------------------------------------------------------|-------------------------------------------------------------------------|-------------------------------------------------------------------------|
| | | | |
| Started | 28 | 7 | 2 |
| Completed | 10 | 5 | 2 |
| Not completed | 18 | 2 | 0 |
| Non-compliance with Study Drug | 2 | - | - |
| Investigator's Discretion | 14 | 1 | - |
| Pregnancy | 1 | - | - |
| Lost to follow-up | 1 | 1 | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------|
| Reporting group title | Main Phase: F/TAF+3rd ARV Agent (Cohort 1) |
| Reporting group description: Participants between 12 to < 18 years of age and ≥ 35 kg body weight received emtricitabine/tenofovir alafenamide (F/TAF) 200/10 mg fixed-dose combination (FDC) tablet (with boosted 3rd antiretroviral [ARV] agent) or F/TAF 200/25 mg FDC tablet (with unboosted 3rd ARV agent) orally once daily for 48 weeks. Allowed boosted 3rd ARV agents: LPV, ATV, DRV; Allowed unboosted 3rd ARV agents: EFV, RAL, DTG, or NVP. | |
| Reporting group title | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 1) |
| 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 protease inhibitor (PI) for 48 weeks. Allowed boosted PIs: ATV, LPV or DRV. | |
| Reporting group title | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 2) |
| 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. Allowed boosted 3rd ARV agents: LPV, ATV, DRV; Allowed unboosted 3rd ARV agents: EFV, RAL, DTG, or NVP. | |

| Reporting group values | Main Phase: F/TAF+3rd ARV Agent (Cohort 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 2) |
|-----------------------------------------------------------------------------------------|--------------------------------------------------|-----------------------------------------------------------------------|-----------------------------------------------------------------------|
| Number of subjects | 28 | 9 | 3 |
| Age categorical Units: Subjects | | | |
| 6 to < 12 years | 0 | 9 | 3 |
| 12 to < 15 years | 19 | 0 | 0 |
| 15 to < 18 years | 9 | 0 | 0 |
| 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 standard deviation | 909 ± 242.7 | 871 ± 364.8 | 1209 ± 306.3 |
| CD4 Percentage (%) Units: Percentage of lymphocytes arithmetic mean standard deviation | 36.1 ± 6.40 | 36.7 ± 4.35 | 36.1 ± 3.35 |

| | | | |
|-----------------------------------------------------------------------------------------------------------|-------|--|--|
| Reporting group values | Total | | |
| Number of subjects | 40 | | |
| Age categorical Units: Subjects | | | |
| 6 to < 12 years | 12 | | |
| 12 to < 15 years | 19 | | |
| 15 to < 18 years | 9 | | |
| 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 | Main Phase: F/TAF+3rd ARV Agent (Cohort 1) |
| Reporting group description: Participants between 12 to < 18 years of age and ≥ 35 kg body weight received emtricitabine/tenofovir alafenamide (F/TAF) 200/10 mg fixed-dose combination (FDC) tablet (with boosted 3rd antiretroviral [ARV] agent) or F/TAF 200/25 mg FDC tablet (with unboosted 3rd ARV agent) orally once daily for 48 weeks. Allowed boosted 3rd ARV agents: LPV, ATV, DRV; Allowed unboosted 3rd ARV agents: EFV, RAL, DTG, or NVP. | |
| Reporting group title | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 1) |
| 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 protease inhibitor (PI) for 48 weeks. Allowed boosted PIs: ATV, LPV or DRV. | |
| Reporting group title | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 2) |
| 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. Allowed boosted 3rd ARV agents: LPV, ATV, DRV; Allowed unboosted 3rd ARV agents: EFV, RAL, DTG, or NVP. | |
| Reporting group title | Extension Phase: F/TAF+3rd ARV Agent (Cohort 1) |
| Reporting group description: After completion of 48 weeks, all participants were given the option to participate in an extension phase of the study to continue with F/TAF+3rd ARV agent. Gilead provided F/TAF until a) the participant turned 18 and F/TAF was commercially available for use in adults in the country in which the participant was enrolled or, b) F/TAF became commercially available for pediatric use in the country in which the participant was enrolled or, c) Gilead Sciences elected to terminate development of F/TAF in the applicable country. The maximum exposure was 438.9 weeks. Allowed boosted 3rd ARV agents: LPV, ATV, DRV; Allowed unboosted 3rd ARV agents: EFV, RAL, DTG, or NVP. | |
| Reporting group title | Extension Phase:F/TAF+3rd ARV Agent (Cohort 2, Part A-Group 1) |
| Reporting group description: After completion of 48 weeks, all participants were given the option to participate in an extension phase of the study to continue with F/TAF+3rd ARV agent. Gilead provided F/TAF until a) the participant turned 18 and F/TAF was commercially available for use in adults in the country in which the participant was enrolled or, b) F/TAF became commercially available for pediatric use in the country in which the participant is enrolled or, c) Gilead Sciences elected to terminate development of F/TAF in the applicable country. The maximum exposure was 315.0 weeks. Allowed boosted PIs: ATV, LPV or DRV. | |
| Reporting group title | Extension Phase:F/TAF+3rd ARV Agent (Cohort 2, Part A-Group 2) |
| Reporting group description: After completion of 48 weeks, all participants were given the option to participate in an extension phase of the study to continue with F/TAF+3rd ARV Agent. Gilead provided F/TAF until a) the participant turned 18 and F/TAF was commercially available for use in adults in the country in which the participant was enrolled or, b) F/TAF became commercially available for pediatric use in the country in which the participant was enrolled or, c) Gilead Sciences elected to terminate development of F/TAF in the applicable country. The maximum exposure was 103.1 weeks. Allowed boosted 3rd ARV agents: LPV, ATV, DRV; Allowed unboosted 3rd ARV agents: EFV, RAL, DTG, or NVP. | |
| Subject analysis set title | Main Phase: 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 were given the option to participate in an extension phase of the study to continue with F/TAF+3rd ARV agent. Gilead provided F/TAF until a) the participant turned 18 and F/TAF was commercially available for use in adults in the country in which the participant was enrolled or, b) F/TAF became commercially available for pediatric use in the country in which the participant was enrolled or, c) Gilead Sciences elected to terminate development of F/TAF in the applicable country. (Allowed boosted 3rd ARV agents: LPV, ATV, DRV). The participants received the study drug up to a maximum of 438.9 weeks. | |

| | |
|----------------------------|------------------------------------------------------|
| Subject analysis set title | Main Phase: 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 \geq 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 were given the option to participate in an extension phase of the study to continue with F/TAF+3rd ARV agent. Gilead provided F/TAF until a) the participant turned 18 and F/TAF was commercially available for use in adults in the country in which the participant was enrolled or, b) F/TAF became commercially available for pediatric use in the country in which the participant was enrolled or, c) Gilead Sciences elected to terminate development of F/TAF in the applicable country. (Allowed unboosted 3rd ARV agents: EFV, RAL, DTG, or NVP). The participants received the study drug up to a maximum of 438.9 weeks.

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

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

End point description:

AUCtau is defined as the area under the drug 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: Only descriptive analyses were planned for this endpoint.

| End point values | Main Phase: F/TAF 200/10 mg+3rd ARV Agent (Cohort 1) | Main Phase: 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 (\pm 113.23) | 200.6 (\pm 83.80) | | |

Statistical analyses

No statistical analyses for this end point

Primary: PK Parameter (Cohort 2: Part A - Groups 1 and 2): AUCtau of TAF

| | |
|-----------------|-----------------------------------------------------------------------------------|
| End point title | PK Parameter (Cohort 2: Part A - Groups 1 and 2): AUCtau of TAF ^{[2][3]} |
|-----------------|-----------------------------------------------------------------------------------|

End point description:

AUCtau is defined as the area under the drug concentration versus time curve over the dosing interval. The IPK 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: Only descriptive analyses were planned for this endpoint.

[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 data for this endpoint is reported separately for Cohorts 1 and 2.

| End point values | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 2) | | |
|--------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|--|--|
| 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: Only descriptive analyses were planned for this endpoint.

| End point values | Main Phase: F/TAF+3rd ARV Agent (Cohort 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 2) | |
|-----------------------------------|-----------------------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|--|
| 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 | Main Phase: F/TAF 200/10 mg+3rd ARV Agent (Cohort 1) | Main Phase: 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: Part A - Groups 1 and 2): Cmax of TAF, FTC, and TFV

| | |
|-----------------|-----------------------------------------------------------|
| End point title | PK Parameter (Cohort 2: Part A - Groups 1 and 2): Cmax of |
|-----------------|-----------------------------------------------------------|

End point description:

Cmax is defined as the maximum concentration of drug. Participants in the IPK 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 data for this endpoint is reported separately for Cohorts 1 and 2.

| End point values | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 2) | | |
|--------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|--|--|
| 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 | Main Phase: F/TAF 200/10 mg+3rd ARV Agent (Cohort 1) | Main Phase: 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: Part A - Groups 1 and 2): Clast of TAF

| | |
|-----------------|------------------------------------------------------------|
| End point title | PK Parameter (Cohort 2: Part A - Groups 1 and 2): Clast of |
|-----------------|------------------------------------------------------------|

End point description:

Clast is defined as the last observable concentration of drug. Participants in the IPK 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 data for this endpoint is reported separately for Cohorts 1 and 2.

| End point values | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 2) | | |
|--------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|--|--|
| 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 clearance following oral 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 | Main Phase: F/TAF 200/10 mg+3rd ARV Agent (Cohort 1) | Main Phase: 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: Part A - Groups 1 and 2): CL/F of TAF

| | |
|-----------------|-----------------------------------------------------------|
| End point title | PK Parameter (Cohort 2: Part A - Groups 1 and 2): CL/F of |
|-----------------|-----------------------------------------------------------|

End point description:

CL/F is defined as the apparent clearance following oral administration of the drug. Participants in the IPK 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 data for this endpoint is reported separately for Cohorts 1 and 2.

| | | | | |
|--------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|--|--|
| End point values | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 2) | | |
| 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 following oral 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 | Main Phase: F/TAF 200/10 mg+3rd ARV Agent (Cohort 1) | Main Phase: 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: Part A - Groups 1 and 2): Vz/F of TAF

| | |
|-----------------|-----------------------------------------------------------|
| End point title | PK Parameter (Cohort 2: Part A - Groups 1 and 2): Vz/F of |
|-----------------|-----------------------------------------------------------|

End point description:

Vz/F is defined as the apparent volume of distribution following oral administration of the drug. Participants in the IPK 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 data for this endpoint is reported separately for Cohorts 1 and 2.

| End point values | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 2) | | |
|--------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|--|--|
| 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 the area under the drug 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 | Main Phase: F/TAF 200/10 mg+3rd ARV Agent (Cohort 1) | Main Phase: 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: Part A - Groups 1 and 2): AUCtau of FTC and TFV

| | |
|-----------------|----------------------------------------------------------------------------------------|
| End point title | PK Parameter (Cohort 2: Part A - Groups 1 and 2): AUCtau of FTC and TFV ^[9] |
|-----------------|----------------------------------------------------------------------------------------|

End point description:

AUCtau is defined as the area under the drug 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 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 data for this endpoint is reported separately for Cohorts 1 and 2.

| End point values | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 2) | | |
|--------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|--|--|
| 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 | Main Phase: F/TAF 200/10 mg+3rd ARV Agent (Cohort 1) | Main Phase: 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: Part A - Groups 1 and 2): Ctau of FTC and TFV

| | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|
| End point title | PK Parameter (Cohort 2: Part A - Groups 1 and 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 IPK 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 data for this endpoint is reported separately for Cohorts 1 and 2.

| End point values | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 2) | | |
|--------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|--|--|
| 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 | Main Phase: F/TAF+3rd ARV Agent (Cohort 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 2) | |
|-----------------------------------|-----------------------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|--|
| 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 | 89.3 | 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 | Main Phase: F/TAF+3rd ARV Agent (Cohort 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 2) | |
|-----------------------------------|-----------------------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|--|
| 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 | Main Phase: F/TAF+3rd ARV Agent (Cohort 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 2) | |
|-----------------------------------|-----------------------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|--|
| 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 | Main Phase: F/TAF+3rd ARV Agent (Cohort 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 2) | |
|--------------------------------------|-----------------------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 28 | 8 | 2 | |
| Units: cells/ μ L | | | | |
| arithmetic mean (standard deviation) | -130 (\pm 272.6) | 68 (\pm 352.5) | -299 (\pm 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 | Main Phase: F/TAF+3rd ARV Agent (Cohort 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 2) | |
|--------------------------------------|-----------------------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 28 | 7 | 2 | |
| Units: cells/ μ L | | | | |
| arithmetic mean (standard deviation) | -105 (\pm 162.9) | 210 (\pm 406.5) | -124 (\pm 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 | Main Phase: F/TAF+3rd ARV Agent (Cohort 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 2) | |
|--------------------------------------|-----------------------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 28 | 8 | 2 | |
| Units: percentage of lymphocytes | | | | |
| arithmetic mean (standard deviation) | -0.21 (\pm | 1.29 (\pm 2.395) | 0.60 (\pm 5.798) | |

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 | Main Phase: F/TAF+3rd ARV Agent (Cohort 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 2) | |
|--------------------------------------|-----------------------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 28 | 7 | 2 | |
| Units: percentage of lymphocytes | | | | |
| arithmetic mean (standard deviation) | -0.20 (± 3.407) | 0.70 (± 3.520) | 3.65 (± 7.283) | |

Statistical analyses

No statistical analyses for this end point

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

| | |
|-----------------|---------------------------------------------------------------|
| End point title | Number of Participants With Palatability of F/TAF Formulation |
|-----------------|---------------------------------------------------------------|

End point description:

Palatability was reported based on the pleasant product taste as 'Yes' or 'No'. Data has been reported for Participant Response (PR) and Guardian Response (GR). Participants with missing data were reported as N/A.

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, '999' 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 | Main Phase: F/TAF+3rd ARV Agent (Cohort 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 2) | |
|----------------------------------------------------|-----------------------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 28 ^[11] | 9 | 3 | |
| Units: Participants | | | | |
| Week 2: PR: Was the Study Drug Palatable? Yes | 25 | 9 | 2 | |
| Week 2: PR: Was the Study Drug Palatable? No | 0 | 0 | 0 | |
| Week 2: PR: Was the Study Drug Palatable? N/A | 3 | 0 | 1 | |
| Week 4: PR: Was the Study Drug Palatable? Yes | 999 | 9 | 3 | |
| Week 4: PR: Was the Study Drug Palatable? No | 999 | 0 | 0 | |
| Week 4: PR: Was the Study Drug Palatable? N/A | 999 | 0 | 0 | |
| Week 2:GR:Study Drug Palatable to Participant? Yes | 11 | 9 | 1 | |
| Week 2:GR:Study Drug Palatable to Participant? No | 0 | 0 | 0 | |
| Week 2:GR:Study Drug Palatable to Participant? N/A | 17 | 0 | 2 | |
| Week 4:GR:Study Drug Palatable to Participant? Yes | 999 | 9 | 1 | |
| Week 4:GR:Study Drug Palatable to Participant? No | 999 | 0 | 0 | |
| Week 4:GR:Study Drug Palatable to Participant? N/A | 999 | 0 | 2 | |
| Week2:GR:Participant Complain Taste of Tablet? Yes | 0 | 0 | 0 | |
| Week2:GR:Participant Complain Taste of Tablet? No | 12 | 9 | 1 | |
| Week2:GR:Participant Complain Taste of Tablet? N/A | 16 | 0 | 2 | |
| Week4:GR:Participant Complain Taste of Tablet? Yes | 999 | 0 | 0 | |
| Week4:GR:Participant Complain Taste of Tablet? No | 999 | 9 | 1 | |
| Week4:GR:Participant Complain Taste of Tablet? N/A | 999 | 0 | 2 | |

Notes:

[11] - 28, 0, 28, 0, 28, 0

Statistical analyses

No statistical analyses for this end point

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

| | |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------|
| End point title | Number of Participants With Acceptability of F/TAF Formulation |
| End point description: | |
| Acceptability has been reported for categories medication size, shape and difficulty swallowing as 'Yes' or 'No' for Participant Response (PR) and Guardian Response (GR). Participants with missing data were reported as N/A. | |
| Participants in the Safety 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 up to Week 4 | |

| End point values | Main Phase: F/TAF+3rd ARV Agent (Cohort 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 1) | Main Phase: F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 2) | |
|----------------------------------------------------|-----------------------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 25 | 9 | 3 | |
| Units: Participants | | | | |
| PR: Was the Study Medication Size Acceptable? Yes | 25 | 9 | 3 | |
| PR: Was the Study Medication Size Acceptable? No | 0 | 0 | 0 | |
| PR: Was the Study Medication Size Acceptable? N/A | 0 | 0 | 0 | |
| PR: Was the Study Medication Shape Acceptable? Yes | 25 | 9 | 3 | |
| PR: Was the Study Medication Shape Acceptable? No | 0 | 0 | 0 | |
| PR: Was the Study Medication Shape Acceptable? NA | 0 | 0 | 0 | |
| GR: Have Difficulty Swallowing Tablet? Yes | 0 | 0 | 0 | |
| GR: Have Difficulty Swallowing Tablet? No | 21 | 9 | 2 | |
| GR: Have Difficulty Swallowing Tablet? N/A | 4 | 0 | 1 | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality: Up to 439 weeks; Adverse events: Up to 410.4 weeks

Adverse event reporting additional description:

All-cause mortality: All Enrolled Analysis Set; AEs: Safety Analysis Set. Cohort 1 data was analyzed together as both treatments were expected to have similar effect on efficacy and safety for target population. AEs are reported together for Main and Extension Phase as participants continued same medication from main to extension phase.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 27.1 |
|--------------------|------|

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 emtricitabine/tenofovir alafenamide (F/TAF) 200/10 mg fixed-dose combination (FDC) tablet (with boosted 3rd antiretroviral [ARV] agent: lopinavir [LPV], atazanavir [ATV], darunavir [DRV]) or F/TAF 200/25 mg FDC tablet (with unboosted 3rd ARV agent: efavirenz [EFV], raltegravir [RAL], dolutegravir [DTG], or nevirapine [NVP]) orally once daily for 48 weeks. After completion of 48 weeks, all participants were given an option to participate in extension phase of study to continue with F/TAF+3rd ARV agent. Gilead provided F/TAF until a) participant turned 18 and F/TAF was commercially available for use in adults in the country in which participant was enrolled or, b) F/TAF became commercially available for pediatric use in the country in which participant was enrolled or, c) Gilead Sciences elected to terminate development of F/TAF in applicable country. Participants received study drug up to a maximum of 438.9 weeks.

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

Reporting group description:

Participants between 2 to < 12 years of age and 17 to < 25 kg body weight received to 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 were given the option to participate in the extension phase of the study to continue with F/TAF+3rd ARV agent. Gilead provided F/TAF until a) the participant turned 18 and F/TAF was commercially available for use in adults in the country in which the participant was enrolled or, b) F/TAF became commercially available for pediatric use in the country in which the participant was enrolled or, c) Gilead Sciences elected 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). The participants received the study drug up to a maximum of 103.1 weeks.

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

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 protease inhibitor (PI) for 48 weeks. After completion of 48 weeks, all participants were given the option to participate in the extension phase of the study to continue with F/TAF+3rd ARV agent. Gilead provided F/TAF until a) the participant turned 18 and F/TAF was commercially available for use in adults in the country in which the participant was enrolled or, b) F/TAF became commercially available for pediatric use in the country in which the participant was enrolled or, c) Gilead Sciences elected to terminate development of F/TAF in the applicable country. (Allowed boosted PIs: ATV, LPV or DRV). The participants received the study drug up to a maximum of 315.0 weeks.

| Serious adverse events | F/TAF+3rd ARV Agent (Cohort 1) | F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 2) | F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 1) |
|---------------------------------------------------|--------------------------------|--------------------------------------------------|--------------------------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 28 (14.29%) | 0 / 3 (0.00%) | 1 / 9 (11.11%) |

| | | | |
|-------------------------------------------------|----------------|---------------|----------------|
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Forearm fracture | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 3 (0.00%) | 0 / 9 (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 |
| Stab wound | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 3 (0.00%) | 0 / 9 (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 |
| Joint dislocation | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 3 (0.00%) | 0 / 9 (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 |
| Nervous system disorders | | | |
| Syncope | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 3 (0.00%) | 0 / 9 (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 / 3 (0.00%) | 0 / 9 (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 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 3 (0.00%) | 1 / 9 (11.11%) |
| 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 | | | |
| Electrolyte imbalance | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 3 (0.00%) | 0 / 9 (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, Part A - Group 2) | F/TAF+3rd ARV Agent (Cohort 2, Part A - Group 1) |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------|------------------------------------------------------------------------|-------------------------------------------------------------------------|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 27 / 28 (96.43%) | 2 / 3 (66.67%) | 8 / 9 (88.89%) |
| Surgical and medical procedures Circumcision subjects affected / exposed occurrences (all) | 2 / 28 (7.14%) 2 | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all) | 2 / 28 (7.14%) 3 | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Reproductive system and breast disorders Balanoposthitis subjects affected / exposed occurrences (all) Dysmenorrhoea subjects affected / exposed occurrences (all) Vaginal discharge subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 2 / 28 (7.14%) 2 2 / 28 (7.14%) 2 | 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 | 1 / 9 (11.11%) 1 0 / 9 (0.00%) 0 0 / 9 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Respiratory symptom subjects affected / exposed occurrences (all) Asthmatic crisis subjects affected / exposed occurrences (all) Oropharyngeal pain | 2 / 28 (7.14%) 2 2 / 28 (7.14%) 4 | 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 0 / 9 (0.00%) 0 |

| | | | |
|--------------------------------------------------------------------------------------------------------------------|----------------------|--------------------|---------------------|
| subjects affected / exposed occurrences (all) | 3 / 28 (10.71%) 3 | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Nasal congestion subjects affected / exposed occurrences (all) | 3 / 28 (10.71%) 3 | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Cough subjects affected / exposed occurrences (all) | 3 / 28 (10.71%) 3 | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Rhinitis allergic subjects affected / exposed occurrences (all) | 4 / 28 (14.29%) 5 | 0 / 3 (0.00%) 0 | 2 / 9 (22.22%) 2 |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) | 3 / 28 (10.71%) 3 | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Depression subjects affected / exposed occurrences (all) | 5 / 28 (17.86%) 6 | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Adjustment disorder subjects affected / exposed occurrences (all) | 2 / 28 (7.14%) 2 | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Investigations Weight decreased subjects affected / exposed occurrences (all) | 5 / 28 (17.86%) 6 | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Blood creatine phosphokinase increased subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 | 0 / 3 (0.00%) 0 | 1 / 9 (11.11%) 1 |
| Vitamin D decreased subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 9 (11.11%) 1 |
| Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all) | 3 / 28 (10.71%) 4 | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Animal bite | | | |

| | | | |
|--------------------------------------|------------------|----------------|----------------|
| subjects affected / exposed | 2 / 28 (7.14%) | 0 / 3 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Muscle strain | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 3 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 1 | 0 | 1 |
| Procedural pain | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 0 / 3 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Heat stroke | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 3 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin laceration | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 1 / 3 (33.33%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Seroma | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 3 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Cardiac disorders | | | |
| Sinus bradycardia | | | |
| subjects affected / exposed | 4 / 28 (14.29%) | 0 / 3 (0.00%) | 2 / 9 (22.22%) |
| occurrences (all) | 4 | 0 | 2 |
| Nervous system disorders | | | |
| Syncope | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 1 / 3 (33.33%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Headache | | | |
| subjects affected / exposed | 13 / 28 (46.43%) | 0 / 3 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 16 | 0 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 6 / 28 (21.43%) | 0 / 3 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 7 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 3 (33.33%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ear and labyrinth disorders | | | |

| | | | |
|------------------------------------------------------------------------------------------------|----------------------|---------------------|---------------------|
| Ear pain subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 1 / 3 (33.33%) 1 | 0 / 9 (0.00%) 0 |
| Eye disorders Eczema eyelids subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 9 (11.11%) 1 |
| Vernal keratoconjunctivitis subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 9 (11.11%) 1 |
| Gastrointestinal disorders Haemorrhoids subjects affected / exposed occurrences (all) | 3 / 28 (10.71%) 4 | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Abdominal pain subjects affected / exposed occurrences (all) | 2 / 28 (7.14%) 3 | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Dyspepsia subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 2 | 0 / 3 (0.00%) 0 | 1 / 9 (11.11%) 1 |
| Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 9 (11.11%) 1 |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 3 / 28 (10.71%) 3 | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Nausea subjects affected / exposed occurrences (all) | 6 / 28 (21.43%) 8 | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Diarrhoea subjects affected / exposed occurrences (all) | 6 / 28 (21.43%) 7 | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Dental caries subjects affected / exposed occurrences (all) | 4 / 28 (14.29%) 4 | 0 / 3 (0.00%) 0 | 2 / 9 (22.22%) 2 |
| Vomiting | | | |

| | | | |
|--------------------------------------------------|-----------------------|--------------------|---------------------|
| subjects affected / exposed occurrences (all) | 7 / 28 (25.00%) 10 | 0 / 3 (0.00%) 0 | 1 / 9 (11.11%) 1 |
| Skin and subcutaneous tissue disorders | | | |
| Rash papular | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 0 / 3 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Dermatitis contact | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 0 / 3 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Dermatitis allergic | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 3 (0.00%) | 2 / 9 (22.22%) |
| occurrences (all) | 0 | 0 | 2 |
| Dermatitis | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 1 / 3 (33.33%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Acne | | | |
| subjects affected / exposed | 8 / 28 (28.57%) | 0 / 3 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 8 | 0 | 1 |
| Renal and urinary disorders | | | |
| Haematuria | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 0 / 3 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Muscle spasms | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 0 / 3 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 2 | 0 | 1 |
| Arthralgia | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 0 / 3 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Back pain | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 0 / 3 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Infections and infestations | | | |
| Pharyngitis | | | |
| subjects affected / exposed | 5 / 28 (17.86%) | 1 / 3 (33.33%) | 1 / 9 (11.11%) |
| occurrences (all) | 5 | 3 | 1 |

| | | | |
|-----------------------------------|------------------|---------------|----------------|
| Influenza | | | |
| subjects affected / exposed | 8 / 28 (28.57%) | 0 / 3 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 13 | 0 | 1 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 13 / 28 (46.43%) | 0 / 3 (0.00%) | 5 / 9 (55.56%) |
| occurrences (all) | 23 | 0 | 18 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 7 / 28 (25.00%) | 0 / 3 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 12 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 4 / 28 (14.29%) | 0 / 3 (0.00%) | 2 / 9 (22.22%) |
| occurrences (all) | 5 | 0 | 2 |
| Body tinea | | | |
| subjects affected / exposed | 4 / 28 (14.29%) | 0 / 3 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Covid-19 | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 0 / 3 (0.00%) | 2 / 9 (22.22%) |
| occurrences (all) | 2 | 0 | 2 |
| Hordeolum | | | |
| subjects affected / exposed | 3 / 28 (10.71%) | 0 / 3 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 3 | 0 | 1 |
| Folliculitis | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 0 / 3 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Conjunctivitis | | | |
| subjects affected / exposed | 3 / 28 (10.71%) | 0 / 3 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 3 / 28 (10.71%) | 0 / 3 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 8 | 0 | 0 |
| Bacterial vaginosis | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 0 / 3 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Acarodermatitis | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 0 / 3 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |

| | | | |
|-----------------------------------------|-----------------|----------------|----------------|
| Tooth abscess | | | |
| subjects affected / exposed | 3 / 28 (10.71%) | 0 / 3 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 2 / 3 (66.67%) | 0 / 9 (0.00%) |
| occurrences (all) | 6 | 3 | 0 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 0 / 3 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Otitis externa | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 3 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 1 | 0 | 1 |
| Otitis media acute | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 0 / 3 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Pharyngotonsillitis | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 3 (0.00%) | 2 / 9 (22.22%) |
| occurrences (all) | 0 | 0 | 2 |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 0 / 3 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 0 / 3 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Tonsillitis | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 0 / 3 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 0 / 3 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Vulvovaginal mycotic infection | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 0 / 3 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Helminthic infection | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 1 / 3 (33.33%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|------------------------------------|-----------------|---------------|---------------|
| Metabolism and nutrition disorders | | | |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 7 / 28 (25.00%) | 0 / 3 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 9 | 0 | 0 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 20 November 2014 | <ul style="list-style-type: none">- 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 | <ul style="list-style-type: none">- 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