



Clinical trial results:

A Phase 3, Randomized, Double-Blind Study to Evaluate the Safety and Efficacy of Fixed Dose Combination of Bictegravir/Emtricitabine/Tenofovir Alafenamide versus Dolutegravir + Emtricitabine/Tenofovir Disoproxil Fumarate in Treatment Naïve, HIV-1 and Hepatitis B Co-Infected Adults

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2018-000926-79 |
| Trial protocol | FR ES GR |
| Global end of trial date | 07 March 2024 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 15 March 2025 |
| First version publication date | 15 March 2025 |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | GS-US-380-4458 |
|-----------------------|----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03547908 |
| 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) | No |
| 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? | No |

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 07 March 2024 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 25 February 2022 |
| Global end of trial reached? | Yes |
| Global end of trial date | 07 March 2024 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the efficacy of fixed-dose combination (FDC) of bicitgravir/emtricitabine/ tenofovir alafenamide (B/F/TAF) versus dolutegravir (DTG) + emtricitabine/tenofovir disoproxil fumarate (F/TDF) in treatment-naïve and HIV-1 and hepatitis B virus (HBV) adults.

Protection of trial subjects:

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

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

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------|
| Actual start date of recruitment | 30 May 2018 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Dominican Republic: 10 |
| Country: Number of subjects enrolled | Malaysia: 37 |
| Country: Number of subjects enrolled | United States: 3 |
| Country: Number of subjects enrolled | Spain: 7 |
| Country: Number of subjects enrolled | Türkiye: 9 |
| Country: Number of subjects enrolled | Hong Kong: 5 |
| Country: Number of subjects enrolled | Puerto Rico: 1 |
| Country: Number of subjects enrolled | Taiwan: 12 |
| Country: Number of subjects enrolled | China: 56 |
| Country: Number of subjects enrolled | Japan: 8 |
| Country: Number of subjects enrolled | Korea, Republic of: 2 |
| Country: Number of subjects enrolled | Thailand: 94 |
| Worldwide total number of subjects | 244 |
| EEA total number of subjects | 7 |

Notes:

| Subjects enrolled per age group | |
|---|-----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 242 |
| From 65 to 84 years | 2 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in the North American, Asian and European regions.

Pre-assignment

Screening details:

381 participants were screened.

Period 1

| | |
|------------------------------|-------------------------|
| Period 1 title | Blinded Phase |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Blinded Phase: B/F/TAF |

Arm description:

Participants who were HIV-1 and HBV co-infected and treatment-naïve received bicitegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) (50/200/25 mg) fixed-dose combination (FDC) tablet orally, once daily without regard to food for 96 weeks. Participants also received placebo to match (PTM) dolutegravir (DTG) tablet and PTM emtricitabine/ tenofovir desoproxil fumarate (F/TDF) tablet orally once daily without regard to food for 96 weeks.

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

Dosage and administration details:

50/200/25 mg fixed-dose combination (FDC) tablet administered once daily, without regard to food.

| | |
|--|------------------------|
| Investigational medicinal product name | Placebo to Match F/TDF |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Administered once daily, without regard to food.

| | |
|--|----------------------|
| Investigational medicinal product name | Placebo to Match DTG |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Administered once daily, without regard to food.

| | |
|------------------|----------------------------|
| Arm title | Blinded Phase: DTG + F/TDF |
|------------------|----------------------------|

Arm description:

Participants who were HIV-1 and HBV co-infected and treatment-naïve received DTG (50 mg) tablet + F/TDF (200/300 mg) FDC tablet, orally, once daily without regard to food for 96 weeks. Participants also received PTM B/F/TAF tablet, orally, once daily without regard to food for 96 weeks.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | DTG |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Administered once daily, without regard to food.

| | |
|--|------------------------|
| Investigational medicinal product name | Placebo to Match F/TDF |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Administered once daily, without regard to food.

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

Dosage and administration details:

Administered once daily, without regard to food.

| Number of subjects in period 1^[1] | Blinded Phase: B/F/TAF | Blinded Phase: DTG + F/TDF |
|---|-------------------------------|-----------------------------------|
| Started | 121 | 122 |
| Completed | 111 | 113 |
| Not completed | 10 | 9 |
| Withdrew Consent | 2 | 3 |
| Adverse Event | 1 | - |
| Death | 2 | - |
| Investigator's Discretion | 2 | 1 |
| Non-Compliance With Study Drug | - | 2 |
| Lost to follow-up | 3 | 3 |

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: One participant was randomized to B/f/TAF group but was not treated.

Period 2

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

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|--|--|
| Arm title | Open-Label Extension Phase: B/F/TAF from B/F/TAF |
| Arm description: | |
| After Week 96, participants continued their blinded study drug and attended visits every 12 weeks until the End of Blinded Treatment Visit. Following the End of Blinded Treatment Visit, if safety and efficacy of B/F/TAF FDC was demonstrated for the HIV-1 and HBV coinfecting participants, in a country where B/F/TAF FDC was not available, participants were given the option to receive 48-weeks of open-label B/F/TAF until the product became accessible through an access program, or until Gilead elected to discontinue the study in that country, whichever occurred first. | |
| Arm type | Experimental |
| Investigational medicinal product name | B/F/TAF |
| Investigational medicinal product code | |
| Other name | Biktarvy® |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

50/200/25 mg B/F/TAF FDC tablet administered once daily, without regard to food.

| | |
|--|--|
| Arm title | Open-Label Extension Phase: B/F/TAF from DTG+F/TDF |
| Arm description: | |
| After Week 96, participants continued their blinded study drug and attended visits every 12 weeks until the End of Blinded Treatment Visit. Following the End of Blinded Treatment Visit, if safety and efficacy of B/F/TAF FDC was demonstrated for the HIV-1 and HBV coinfecting participants, in a country where B/F/TAF FDC was not available, participants were given the option to receive 48-weeks of open-label B/F/TAF until the product became accessible through an access program, or until Gilead elected to discontinue the study in that country, whichever occurred first. | |
| Arm type | Experimental |
| Investigational medicinal product name | B/F/TAF |
| Investigational medicinal product code | |
| Other name | Biktarvy® |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

50/200/25 mg B/F/TAF FDC tablet administered once daily, without regard to food.

| Number of subjects in period 2^[2] | Open-Label Extension Phase: B/F/TAF from B/F/TAF | Open-Label Extension Phase: B/F/TAF from DTG+F/TDF |
|---|--|--|
| Started | 95 | 89 |
| Completed | 91 | 88 |
| Not completed | 4 | 1 |
| Death | 1 | - |
| Lost to follow-up | 3 | 1 |

Notes:

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

Justification: Out of 111 (B/F/TAF) and 113 (DTG + F/TDF) participants who completed the Blinded Phase, 95 participants from B/F/TAF and 89 participants from DTG + F/TDF entered the Open-label Extension Phase.

Baseline characteristics

Reporting groups

| | |
|--|----------------------------|
| Reporting group title | Blinded Phase: B/F/TAF |
| Reporting group description: | |
| Participants who were HIV-1 and HBV co-infected and treatment-naïve received bicitgravir/emtricitabine/tenofovir alafenamide (B/F/TAF) (50/200/25 mg) fixed-dose combination (FDC) tablet orally, once daily without regard to food for 96 weeks. Participants also received placebo to match (PTM) dolutegravir (DTG) tablet and PTM emtricitabine/ tenofovir desoproxil fumarate (F/TDF) tablet orally once daily without regard to food for 96 weeks. | |
| Reporting group title | Blinded Phase: DTG + F/TDF |
| Reporting group description: | |
| Participants who were HIV-1 and HBV co-infected and treatment-naïve received DTG (50 mg) tablet + F/TDF (200/300 mg) FDC tablet, orally, once daily without regard to food for 96 weeks. Participants also received PTM B/F/TAF tablet, orally, once daily without regard to food for 96 weeks. | |

| Reporting group values | Blinded Phase: B/F/TAF | Blinded Phase: DTG + F/TDF | Total |
|--------------------------------|------------------------|----------------------------|-------|
| Number of subjects | 121 | 122 | 243 |
| Age categorical | | | |
| Units: Subjects | | | |
| Between 18 and 65 years | 120 | 121 | 241 |
| >=65 years | 1 | 1 | 2 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | ± | ± | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 9 | 2 | 11 |
| Male | 112 | 120 | 232 |
| Race | | | |
| Units: Subjects | | | |
| Asian | 108 | 106 | 214 |
| White | 10 | 9 | 19 |
| Black | 2 | 6 | 8 |
| Other | 1 | 1 | 2 |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 7 | 10 | 17 |
| Not Hispanic or Latino | 114 | 112 | 226 |
| CD4 Percentage | | | |
| Units: percentage of CD4 cells | | | |
| arithmetic mean | | 14.8 | |
| standard deviation | ± | ± 8.25 | - |
| CD4 Cell Count | | | |
| Units: cells/μL | | | |
| arithmetic mean | | 266 | |
| standard deviation | ± | ± 194.3 | - |

Subject analysis sets

| | |
|----------------------------|------------------------|
| Subject analysis set title | Blinded Phase: B/F/TAF |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Participants who were HIV-1 and HBV coinfecting and treatment-naïve received Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) (50/200/25 mg) fixed-dose combination (FDC) tablet orally, once daily without regard to food for 96 weeks. Participants also received placebo to match (PTM) dolutegravir (DTG) tablet and PTM emtricitabine/ tenofovir desoproxil fumarate (F/TDF) tablet orally once daily without regard to food for 96 weeks.

| Reporting group values | Blinded Phase: B/F/TAF | | |
|---|---------------------------|--|--|
| Number of subjects | 121 | | |
| Age categorical Units: Subjects | | | |
| Between 18 and 65 years >=65 years | | | |
| Age continuous Units: years arithmetic mean standard deviation | 33 ± 9.2 | | |
| Gender categorical Units: Subjects | | | |
| Female Male | | | |
| Race Units: Subjects | | | |
| Asian White Black Other | | | |
| Ethnicity Units: Subjects | | | |
| Hispanic or Latino Not Hispanic or Latino | | | |
| CD4 Percentage Units: percentage of CD4 cells arithmetic mean standard deviation | 16.0 ± 8.62 | | |
| CD4 Cell Count Units: cells/μL arithmetic mean standard deviation | 282 ± 193.1 | | |

End points

End points reporting groups

| | |
|--|--|
| Reporting group title | Blinded Phase: B/F/TAF |
| Reporting group description: Participants who were HIV-1 and HBV co-infected and treatment-naïve received bicitgravir/emtricitabine/tenofovir alafenamide (B/F/TAF) (50/200/25 mg) fixed-dose combination (FDC) tablet orally, once daily without regard to food for 96 weeks. Participants also received placebo to match (PTM) dolutegravir (DTG) tablet and PTM emtricitabine/ tenofovir desoproxil fumarate (F/TDF) tablet orally once daily without regard to food for 96 weeks. | |
| Reporting group title | Blinded Phase: DTG + F/TDF |
| Reporting group description: Participants who were HIV-1 and HBV co-infected and treatment-naïve received DTG (50 mg) tablet + F/TDF (200/300 mg) FDC tablet, orally, once daily without regard to food for 96 weeks. Participants also received PTM B/F/TAF tablet, orally, once daily without regard to food for 96 weeks. | |
| Reporting group title | Open-Label Extension Phase: B/F/TAF from B/F/TAF |
| Reporting group description: After Week 96, participants continued their blinded study drug and attended visits every 12 weeks until the End of Blinded Treatment Visit. Following the End of Blinded Treatment Visit, if safety and efficacy of B/F/TAF FDC was demonstrated for the HIV-1 and HBV coinfecting participants, in a country where B/F/TAF FDC was not available, participants were given the option to receive 48-weeks of open-label B/F/TAF until the product became accessible through an access program, or until Gilead elected to discontinue the study in that country, whichever occurred first. | |
| Reporting group title | Open-Label Extension Phase: B/F/TAF from DTG+F/TDF |
| Reporting group description: After Week 96, participants continued their blinded study drug and attended visits every 12 weeks until the End of Blinded Treatment Visit. Following the End of Blinded Treatment Visit, if safety and efficacy of B/F/TAF FDC was demonstrated for the HIV-1 and HBV coinfecting participants, in a country where B/F/TAF FDC was not available, participants were given the option to receive 48-weeks of open-label B/F/TAF until the product became accessible through an access program, or until Gilead elected to discontinue the study in that country, whichever occurred first. | |
| Subject analysis set title | Blinded Phase: B/F/TAF |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Participants who were HIV-1 and HBV coinfecting and treatment-naïve received Bicitgravir/emtricitabine/tenofovir alafenamide (B/F/TAF) (50/200/25 mg) fixed-dose combination (FDC) tablet orally, once daily without regard to food for 96 weeks. Participants also received placebo to match (PTM) dolutegravir (DTG) tablet and PTM emtricitabine/ tenofovir desoproxil fumarate (F/TDF) tablet orally once daily without regard to food for 96 weeks. | |

Primary: Percentage of Participants With Plasma Hepatitis B Virus (HBV) DNA < 29 IU/mL at Week 48 as Defined by Missing = Failure Approach (Co-primary Endpoint)

| | |
|--|---|
| End point title | Percentage of Participants With Plasma Hepatitis B Virus (HBV) DNA < 29 IU/mL at Week 48 as Defined by Missing = Failure Approach (Co-primary Endpoint) |
| End point description: This outcome measure was analyzed using a Missing = Failure approach. In this approach, all missing data were treated as HBV DNA \geq 29 IU/mL. Participants in the Full Analysis Set were analyzed. | |
| End point type | Primary |
| End point timeframe: Week 48 | |

| End point values | Blinded Phase: B/F/TAF | Blinded Phase: DTG + F/TDF | | |
|-----------------------------------|------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 119 | 122 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 63.0 | 43.4 | | |

Statistical analyses

| Statistical analysis title | Plasma Hepatitis B Virus (HBV) DNA < 29 IU/mL |
|----------------------------|---|
|----------------------------|---|

Statistical analysis description:

A sample size of 240 participants provided 81% power to detect a non-inferiority margin of 12% between the 2 treatment groups. This assumed that both treatment groups have a response rate of 88% (based on Gilead Studies GS-US-320-0108 and GS-US-320-0110), that the non-inferiority margin is 12%, and that the significance level of the test is at a one-sided 0.025 level.

| | |
|---|---|
| Comparison groups | Blinded Phase: DTG + F/TDF v Blinded Phase: B/F/TAF |
| Number of subjects included in analysis | 241 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[1] |
| Parameter estimate | Difference in Percentages |
| Point estimate | 16.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 5.9 |
| upper limit | 27.3 |

Notes:

[1] - The difference in percentages of participants with HBV DNA < 29 IU/mL between treatment groups and its 95.001% CI were calculated based on the MH proportions adjusted by baseline HBeAg status (positive vs negative) and baseline HBV DNA category (< 8 log10 IU/mL vs ≥ 8 log10 IU/mL).

| | |
|---|---|
| Statistical analysis title | Plasma Hepatitis B Virus (HBV) DNA < 29 IU/mL |
| Comparison groups | Blinded Phase: DTG + F/TDF v Blinded Phase: B/F/TAF |
| Number of subjects included in analysis | 241 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0023 ^[2] |
| Method | Cochran-Mantel-Haenszel |

Notes:

[2] - The p-value was from CMH test stratified by baseline HBeAg status (positive vs negative) and HBV DNA category (< 8 log10 IU/mL vs ≥ 8 log10 IU/mL).

Primary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 48 as Defined by the US FDA-Defined Snapshot Algorithm (Co-primary Endpoint)

| | |
|-----------------|---|
| 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 (Co-primary Endpoint) |
|-----------------|---|

End point description:

The percentage of participants achieving HIV-1 RNA < 50 copies/mL at Week 48 was analyzed using the snapshot algorithm, which defines 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. Percentages were rounded off.

The Full Analysis Set included all participants who were randomized into the study, received at least 1 dose of study drug, and had at least 1 postbaseline HIV-1 RNA or HBV DNA result while on study drug.

| | |
|----------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| Week 48 | |

| End point values | Blinded Phase: B/F/TAF | Blinded Phase: DTG + F/TDF | | |
|-----------------------------------|------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 119 | 122 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 95.0 | 91.0 | | |

Statistical analyses

| Statistical analysis title | HIV-1 RNA < 50 Copies/mL at Week 48 |
|----------------------------|-------------------------------------|
|----------------------------|-------------------------------------|

Statistical analysis description:

The difference in percentages of participants between groups and their 95.001% confidence intervals (CI)s were calculated based on Mantel-Haenszel (MH) proportions adjusted by baseline HIV-1 RNA stratum ($\leq 100,000$ vs. $> 100,000$ copies/mL).

| | |
|---|---|
| Comparison groups | Blinded Phase: DTG + F/TDF v Blinded Phase: B/F/TAF |
| Number of subjects included in analysis | 241 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[3] |
| Parameter estimate | Difference in Percentages |
| Point estimate | 4.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.5 |
| upper limit | 10.8 |

Notes:

[3] - A sample size of 240 participants randomized in a 1:1 ratio to 2 treatment groups, achieved 90% power to detect a non-inferiority margin of 12% between the 2 treatment groups. For the sample size and power computation, it is assumed that both treatment groups have a response rate of 91% (based on Gilead Studies GS-US-380-1489 and GS-US-380-1490), that the non-inferiority margin is 12%, and that the significance level of the test is at a one-sided 0.025 level.

| Statistical analysis title | HIV-1 RNA < 50 Copies/mL at Week 48 |
|---|---|
| Comparison groups | Blinded Phase: DTG + F/TDF v Blinded Phase: B/F/TAF |
| Number of subjects included in analysis | 241 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2113 ^[4] |
| Method | Cochran-Mantel-Haenszel |

Notes:

[4] - The p-value was calculated from Cochran-Mantel-Haenszel (CMH) test stratified by baseline HIV-1 RNA stratum ($\leq 100,000$ vs. $> 100,000$ copies/mL).

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. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 48 | |

| End point values | Blinded Phase: B/F/TAF | Blinded Phase: DTG + F/TDF | | |
|--------------------------------------|---------------------------|-------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 117 | 116 | | |
| Units: cells/ μ L | | | | |
| arithmetic mean (standard deviation) | 200 (\pm 139.3) | 175 (\pm 124.7) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Change from Baseline in CD4 Cell Count at Week 48 |
| Comparison groups | Blinded Phase: DTG + F/TDF v Blinded Phase: B/F/TAF |
| Number of subjects included in analysis | 233 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[5] |
| P-value | = 0.1701 ^[6] |
| Method | ANOVA |
| Parameter estimate | Difference in least squares mean (LSM) |
| Point estimate | 24 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10 |
| upper limit | 58 |

Notes:

[5] - The difference in least squares means and its 95% CI were calculated using ANOVA model adjusted by the baseline HIV-1 RNA stratum (\leq 100,000 vs. $>$ 100,000 copies/mL).

[6] - The p-value was calculated using ANOVA model adjusted by the baseline HIV-1 RNA stratum (\leq 100,000 vs. $>$ 100,000 copies/mL).

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 96 as Defined by the US FDA-Defined Snapshot Algorithm

| | |
|-----------------|---|
| End point title | Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 96 as Defined by the US FDA-Defined Snapshot Algorithm |
|-----------------|---|

End point description:

The percentage of participants achieving HIV-1 RNA < 50 copies/mL at Week 96 was analyzed using the snapshot algorithm, which was defined as 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. Percentages were rounded off.

Participants in the Full Analysis Set were analyzed.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 96 | |

| End point values | Blinded Phase: B/F/TAF | Blinded Phase: DTG + F/TDF | | |
|-----------------------------------|---------------------------|-------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 119 | 122 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 87.4 | 87.7 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | HIV-1 RNA < 50 Copies/mL at Week 96 |
| Comparison groups | Blinded Phase: B/F/TAF v Blinded Phase: DTG + F/TDF |
| Number of subjects included in analysis | 241 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[7] |
| P-value | = 0.9427 ^[8] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Difference in Percentages |
| Point estimate | -0.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.9 |
| upper limit | 8.3 |

Notes:

[7] - The difference in percentages of participants with HIV-1 RNA < 50 copies/mL between treatment groups and its 95% CI were calculated based on the MH proportions adjusted by baseline HIV-1 RNA stratum ($\leq 100,000$ vs $> 100,000$ copies/mL).

[8] - P-value for the superiority test comparing the percentages of participants with HIV-1 RNA < 50 copies/mL between treatment groups was from the CMH test stratified by baseline HIV-1 RNA stratum ($\leq 100,000$ vs $> 100,000$ copies/mL).

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. |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 48 | |

| End point values | Blinded Phase: B/F/TAF | Blinded Phase: DTG + F/TDF | | |
|--------------------------------------|------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 117 | 116 | | |
| Units: percentage of CD4 cells | | | | |
| arithmetic mean (standard deviation) | 8.43 (± 4.1) | 7.75 (± 4.3) | | |

Statistical analyses

| Statistical analysis title | Change from Baseline in CD4 Percentage at Week 48 |
|---|---|
| Comparison groups | Blinded Phase: DTG + F/TDF v Blinded Phase: B/F/TAF |
| Number of subjects included in analysis | 233 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[9] |
| P-value | = 0.2839 ^[10] |
| Method | ANOVA |
| Parameter estimate | Difference in least squares mean (LSM) |
| Point estimate | 0.59 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.49 |
| upper limit | 1.67 |

Notes:

[9] - The difference in least squares means and its 95% CI were calculated using ANOVA model adjusted by the baseline HIV-1 RNA stratum ($\leq 100,000$ vs. $> 100,000$ copies/mL).

[10] - The p-value was calculated using ANOVA model adjusted by the baseline HIV-1 RNA stratum ($\leq 100,000$ vs. $> 100,000$ copies/mL).

Secondary: Change from Baseline in CD4 Cell Count at Week 96

| | |
|--|---|
| End point title | Change from Baseline in CD4 Cell Count at Week 96 |
| End point description: | |
| Participants in the Full Analysis Set with available data were analyzed. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 96 | |

| End point values | Blinded Phase: B/F/TAF | Blinded Phase: DTG + F/TDF | | |
|--------------------------------------|------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 109 | 113 | | |
| Units: cells/uL | | | | |
| arithmetic mean (standard deviation) | 261 (± 161.6) | 229 (± 174.0) | | |

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Change From Baseline in CD4 Cell Count at Week 96 |
| Statistical analysis description: | |
| Difference in least squares means (Diff in LSM) and its 95% CI were from ANOVA model adjusted by the baseline HIV-1 RNA stratum ($\leq 100,000$ vs. $> 100,000$ copies/mL). | |
| Comparison groups | Blinded Phase: B/F/TAF v Blinded Phase: DTG + F/TDF |
| Number of subjects included in analysis | 222 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.1853 ^[11] |
| Method | ANOVA |
| Parameter estimate | Difference in Least Squares Means |
| Point estimate | 30 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -14 |
| upper limit | 74 |

Notes:

[11] - P-value was from ANOVA model adjusted by the baseline HIV-1 RNA stratum ($\leq 100,000$ vs. $> 100,000$ copies/mL).

Secondary: Percentage of Participants With Plasma HBV DNA < 29 IU/mL at Week 96

| | |
|--|--|
| End point title | Percentage of Participants With Plasma HBV DNA < 29 IU/mL at Week 96 |
| End point description: | |
| This outcome measure was analyzed using a Missing = Failure approach. In this approach, all missing data were treated as HBV DNA ≥ 29 IU/mL. Percentages were rounded-off. Participants in the Full Analysis Set were analyzed. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 96 | |

| End point values | Blinded Phase: B/F/TAF | Blinded Phase: DTG + F/TDF | | |
|-----------------------------------|------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 119 | 122 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 74.8 | 70.5 | | |

Statistical analyses

| | |
|-----------------------------------|---|
| Statistical analysis title | Plasma HBV DNA < 29 IU/mL at Week 96 |
| Comparison groups | Blinded Phase: B/F/TAF v Blinded Phase: DTG + F/TDF |

| | |
|---|-----------------------------|
| Number of subjects included in analysis | 241 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[12] |
| P-value | = 0.6367 ^[13] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Difference in Percentages |
| Point estimate | 2.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.3 |
| upper limit | 13.4 |

Notes:

[12] - The difference in percentages of participants with HBV DNA < 29 IU/mL between treatment groups and its 95% CI were calculated based on the MH proportions adjusted by baseline HBeAg status (positive vs negative) and baseline HBV DNA category (< 8 log₁₀ IU/mL vs ≥ 8 log₁₀ IU/mL).

[13] - P value for the superiority test comparing the percentages of participants with HBV DNA < 29 IU/mL between treatment groups was from CMH test stratified by baseline HBeAg status (positive vs negative) and baseline HBV DNA category (< 8 log₁₀ IU/mL).

Secondary: Change from Baseline in CD4 Percentage at Week 96

| | |
|--|---|
| End point title | Change from Baseline in CD4 Percentage at Week 96 |
| End point description: | |
| Participants in the Full Analysis Set with available data were analyzed. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 96 | |

| End point values | Blinded Phase: B/F/TAF | Blinded Phase: DTG + F/TDF | | |
|--------------------------------------|---------------------------|-------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 108 | 112 | | |
| Units: percentage of CD4 cells | | | | |
| arithmetic mean (standard deviation) | 10.69 (± 5.047) | 10.42 (± 5.096) | | |

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Change From Baseline in CD4 Percentage at Week 96 |
| Statistical analysis description: | |
| Difference in LSM and its 95% CI were from ANOVA model adjusted by the baseline HIV-1 RNA stratum (≤ 100,000 vs. > 100,000 copies/mL). | |
| Comparison groups | Blinded Phase: B/F/TAF v Blinded Phase: DTG + F/TDF |

| | |
|---|--------------------------|
| Number of subjects included in analysis | 220 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.8456 ^[14] |
| Method | ANOVA |
| Parameter estimate | Difference in LSM |
| Point estimate | 0.13 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.2 |
| upper limit | 1.46 |

Notes:

[14] - P-value was from ANOVA model adjusted by the baseline HIV-1 RNA stratum ($\leq 100,000$ vs. $> 100,000$ copies/mL).

Secondary: Percentage of Participants With Alanine Aminotransferase (ALT) Normalization at Week 48 by American Association for the Study of Liver Diseases (AASLD) Criteria

| | |
|-----------------|--|
| End point title | Percentage of Participants With Alanine Aminotransferase (ALT) Normalization at Week 48 by American Association for the Study of Liver Diseases (AASLD) Criteria |
|-----------------|--|

End point description:

ALT normalization was defined as an ALT value that changed from above the normal range at baseline to within the normal range at the given post baseline visit. The upper limit of the normal range (ULN) for ALT using the 2018 AASLD normal range was ≤ 25 U/L for females and ≤ 35 U/L for males. The Missing = Failure approach was used for this analysis. Percentages were rounded off. Participants in the Full Analysis Set with Baseline ALT $>$ ULN were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 48

| End point values | Blinded Phase: B/F/TAF | Blinded Phase: DTG + F/TDF | | |
|-----------------------------------|------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 60 | 47 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 73.3 | 55.3 | | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | ALT Normalization at Week 48 |
| Comparison groups | Blinded Phase: DTG + F/TDF v Blinded Phase: B/F/TAF |

| | |
|---|---------------------------|
| Number of subjects included in analysis | 107 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[15] |
| P-value | = 0.0655 ^[16] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Difference in Percentages |
| Point estimate | 17.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.5 |
| upper limit | 35.7 |

Notes:

[15] - The difference in percentages of participants between groups and their 95% CIs were calculated based on MH proportions adjusted by baseline HBeAg status (positive vs negative) and baseline HBV DNA (< 8 log₁₀ IU/mL vs ≥ 8 log₁₀ IU/mL).

[16] - P-value was calculated from CMH tests stratified by baseline HBeAg status (positive vs negative) and HBV DNA (< 8 log₁₀ IU/mL vs ≥ 8 log₁₀ IU/mL).

Secondary: Percentage of Participants With ALT Normalization at Week 96

| | |
|--|--|
| End point title | Percentage of Participants With ALT Normalization at Week 96 |
| End point description: | |
| ALT normalization was defined as an ALT value that changed from above the normal range at baseline to within the normal range at the given post baseline visit. The upper limit of the normal range (ULN) for ALT using the 2018 AASLD normal range was ≤ 25 U/L for females and ≤ 35 U/L for males. The Missing = Failure approach was used for this analysis. Percentages were rounded-off. Participants in the Full Analysis Set with Baseline ALT > ULN were analyzed. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 96 | |

| End point values | Blinded Phase: B/F/TAF | Blinded Phase: DTG + F/TDF | | |
|-----------------------------------|------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 60 | 47 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 71.7 | 57.4 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | ALT Normalization at Week 96 |
| Comparison groups | Blinded Phase: B/F/TAF v Blinded Phase: DTG + F/TDF |
| Number of subjects included in analysis | 107 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[17] |
| P-value | = 0.1253 ^[18] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Difference in Percentages |
| Point estimate | 14.1 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.3 |
| upper limit | 32.6 |

Notes:

[17] - Difference in the proportion between treatment groups and its 95% CI were calculated based on the MH proportions adjusted by baseline HBeAg status (positive vs negative) and baseline HBV DNA (< 8 log10 IU/mL vs ≥ 8 log10 IU/mL).

[18] - P-value was from the CMH tests stratified by baseline HBeAg status (positive vs negative) and baseline HBV DNA (< 8 log10 IU/mL vs ≥ 8 log10 IU/mL).

Secondary: Percentage of Participants With Hepatitis B Surface Antigen (HBsAg) Loss at Week 48

| | |
|-----------------|---|
| End point title | Percentage of Participants With Hepatitis B Surface Antigen (HBsAg) Loss at Week 48 |
|-----------------|---|

End point description:

HBsAg loss was defined as qualitative HBsAg changing from positive at baseline to negative at a post baseline visit. HBsAg seroconversion was defined as HBsAg loss and HBsAb changes from negative or missing at baseline to positive at a post baseline visit. The Missing = Failure approach was used for this analysis. Percentages were rounded-off.

The Serologically Evaluable Full Analysis Set for HBsAg loss/seroconversion included all participants who were in the Full Analysis Set and with HBsAg positive and HBsAb negative or missing at baseline.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 48

| End point values | Blinded Phase: B/F/TAF | Blinded Phase: DTG + F/TDF | | |
|-----------------------------------|------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 119 | 121 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 12.6 | 5.8 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Hepatitis B Surface Antigen (HBsAg) Loss |
| Comparison groups | Blinded Phase: DTG + F/TDF v Blinded Phase: B/F/TAF |
| Number of subjects included in analysis | 240 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[19] |
| P-value | = 0.0591 ^[20] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Difference in Percentages |
| Point estimate | 7.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.8 |
| upper limit | 15 |

Notes:

[19] - Difference in the percentages between treatment groups and its 95% CI were calculated based on the MH proportions adjusted by baseline HBeAg status (positive vs negative) and baseline HBV DNA ($< 8 \log_{10}$ IU/mL vs $\geq 8 \log_{10}$ IU/mL).

[20] - P-value was from the CMH tests stratified by baseline HBeAg status (positive vs negative) and baseline HBV DNA ($< 8 \log_{10}$ IU/mL vs $\geq 8 \log_{10}$ IU/mL).

Secondary: Percentage of Participants With HBsAg Loss at Week 96

| | |
|--|---|
| End point title | Percentage of Participants With HBsAg Loss at Week 96 |
| End point description: | |
| HBsAg loss was defined as qualitative HBsAg changing from positive at baseline to negative at a post baseline visit. HBsAg seroconversion was defined as HBsAg loss and HBsAb changes from negative or missing at baseline to positive at a post baseline visit. The Missing = Failure approach was used for this analysis. Percentages were rounded-off. Participants in the Serologically Evaluable Full Analysis Set were analyzed. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 96 | |

| End point values | Blinded Phase: B/F/TAF | Blinded Phase: DTG + F/TDF | | |
|-----------------------------------|------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 119 | 121 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 22.7 | 14.0 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | HBsAg Loss at Week 96 |
| Comparison groups | Blinded Phase: B/F/TAF v Blinded Phase: DTG + F/TDF |
| Number of subjects included in analysis | 240 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[21] |
| P-value | = 0.0655 ^[22] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Difference in Percentages |
| Point estimate | 9.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.7 |
| upper limit | 19.2 |

Notes:

[21] - Differences in percentages between treatment groups and their 95% CI were calculated based on MH proportions adjusted by baseline HBeAg status (positive vs negative) and baseline HBV DNA ($< 8 \log_{10}$ IU/mL vs $\geq 8 \log_{10}$ IU/mL).

[22] - P value was from the CMH test stratified by baseline HBeAg status (positive vs negative) and baseline HBV DNA ($< 8 \log_{10}$ IU/mL vs $\geq 8 \log_{10}$ IU/mL). Statistically significant values are shown in bold.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events: Up to the last dose date plus 30 days (maximum exposure: 5.1 years); All-Cause Mortality: Up to 5.3 years

Adverse event reporting additional description:

All-Cause Mortality: All Randomized Analysis Set included all participants who were randomized into the study.

Adverse Events: The Safety Analysis Set included participants who were randomized into the study and received at least 1 dose of study drug.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 26.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------|
| Reporting group title | Blinded B/F/TAF |
|-----------------------|-----------------|

Reporting group description:

Participants who were HIV-1 and HBV coinfecting treatment-naïve received Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) (50/200/25 mg) fixed-dose combination (FDC) tablet orally, once daily without regard to food for 96 weeks. Participants received placebo to match (PTM) dolutegravir (DTG) tablet and PTM emtricitabine/ tenofovir desoproxil fumarate (F/TDF) tablet orally once daily without regard to food for 96 weeks.

| | |
|-----------------------|-----------------------------|
| Reporting group title | OL B/F/TAF from DTG + F/TDF |
|-----------------------|-----------------------------|

Reporting group description:

After Week 96, participants continued their blinded study drug and attended visits every 12 weeks until the End of Blinded Treatment Visit. Following the End of Blinded Treatment Visit, if safety and efficacy of B/F/TAF FDC was demonstrated for the HIV-1 and HBV coinfecting participants, in a country where B/F/TAF FDC was not available, participants were given the option to receive open-label B/F/TAF until the product became accessible through an access program, or until Gilead elected to discontinue the study in that country, whichever occurred first.

| | |
|-----------------------|-------------------------|
| Reporting group title | OL B/F/TAF from B/F/TAF |
|-----------------------|-------------------------|

Reporting group description:

After Week 96, participants continued their blinded study drug and attended visits every 12 weeks until the End of Blinded Treatment Visit. Following the End of Blinded Treatment Visit, if safety and efficacy of B/F/TAF FDC was demonstrated for the HIV-1 and HBV coinfecting participants, in a country where B/F/TAF FDC was not available, participants were given the option to receive open-label B/F/TAF until the product became accessible through an access program, or until Gilead elected to discontinue the study in that country, whichever occurred first.

| | |
|-----------------------|---------------------|
| Reporting group title | Blinded DTG + F/TDF |
|-----------------------|---------------------|

Reporting group description:

Participants who were HIV-1 and HBV coinfecting treatment-naïve received DTG (50 mg) tablet + F/TDF (200/300 mg) FDC tablet, orally, once daily without regard to food for 96 weeks. Participants received PTM B/F/TAF tablet, orally, once daily without regard to food for 96 weeks.

| Serious adverse events | Blinded B/F/TAF | OL B/F/TAF from DTG + F/TDF | OL B/F/TAF from B/F/TAF |
|---|-------------------|-----------------------------|-------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 17 / 121 (14.05%) | 2 / 89 (2.25%) | 4 / 95 (4.21%) |
| number of deaths (all causes) | 2 | 0 | 1 |
| number of deaths resulting from adverse events | | | |

| | | | |
|---|-----------------|----------------|----------------|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Laryngeal squamous cell carcinoma | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 89 (0.00%) | 0 / 95 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Sinonasal papilloma | | | |
| subjects affected / exposed | 0 / 121 (0.00%) | 0 / 89 (0.00%) | 0 / 95 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Glottis carcinoma | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 89 (0.00%) | 0 / 95 (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 |
| Adenocarcinoma of colon | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 89 (0.00%) | 0 / 95 (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 |
| Hepatocellular carcinoma | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 89 (0.00%) | 0 / 95 (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 |
| Injury, poisoning and procedural complications | | | |
| Femoral neck fracture | | | |
| subjects affected / exposed | 0 / 121 (0.00%) | 0 / 89 (0.00%) | 0 / 95 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 121 (0.00%) | 0 / 89 (0.00%) | 0 / 95 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Myocardial ischaemia | | | |

| | | | |
|--|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 89 (0.00%) | 0 / 95 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Alcoholic seizure | | | |
| subjects affected / exposed | 0 / 121 (0.00%) | 1 / 89 (1.12%) | 0 / 95 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 121 (0.00%) | 0 / 89 (0.00%) | 0 / 95 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Death, not otherwise specified | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 89 (0.00%) | 0 / 95 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 89 (0.00%) | 0 / 95 (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 |
| Eye disorders | | | |
| Rhegmatogenous retinal detachment | | | |
| subjects affected / exposed | 0 / 121 (0.00%) | 0 / 89 (0.00%) | 0 / 95 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Haemorrhoids thrombosed | | | |
| subjects affected / exposed | 0 / 121 (0.00%) | 0 / 89 (0.00%) | 1 / 95 (1.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enteritis | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 121 (0.00%) | 0 / 89 (0.00%) | 0 / 95 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 121 (0.00%) | 0 / 89 (0.00%) | 2 / 95 (2.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anal fistula | | | |
| subjects affected / exposed | 0 / 121 (0.00%) | 0 / 89 (0.00%) | 0 / 95 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 121 (0.00%) | 0 / 89 (0.00%) | 0 / 95 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lumbar hernia | | | |
| subjects affected / exposed | 0 / 121 (0.00%) | 0 / 89 (0.00%) | 0 / 95 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Irritable bowel syndrome | | | |
| subjects affected / exposed | 0 / 121 (0.00%) | 0 / 89 (0.00%) | 0 / 95 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 89 (0.00%) | 0 / 95 (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 |
| Skin and subcutaneous tissue disorders | | | |
| Dermal cyst | | | |
| subjects affected / exposed | 0 / 121 (0.00%) | 0 / 89 (0.00%) | 1 / 95 (1.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|----------------|----------------|
| Psychiatric disorders | | | |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 121 (0.00%) | 0 / 89 (0.00%) | 0 / 95 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Bacterial sepsis | | | |
| subjects affected / exposed | 0 / 121 (0.00%) | 1 / 89 (1.12%) | 0 / 95 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anal abscess | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 89 (0.00%) | 1 / 95 (1.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 89 (0.00%) | 0 / 95 (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 |
| Covid-19 | | | |
| subjects affected / exposed | 3 / 121 (2.48%) | 0 / 89 (0.00%) | 0 / 95 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cytomegalovirus chorioretinitis | | | |
| subjects affected / exposed | 0 / 121 (0.00%) | 0 / 89 (0.00%) | 0 / 95 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dengue haemorrhagic fever | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 89 (0.00%) | 0 / 95 (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 |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 89 (0.00%) | 0 / 95 (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 |

| | | | |
|---|-----------------|----------------|----------------|
| Mycotoxycosis | | | |
| subjects affected / exposed | 0 / 121 (0.00%) | 0 / 89 (0.00%) | 0 / 95 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Orchitis | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 89 (0.00%) | 0 / 95 (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 |
| Pneumocystis jirovecii pneumonia | | | |
| subjects affected / exposed | 0 / 121 (0.00%) | 1 / 89 (1.12%) | 0 / 95 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 89 (0.00%) | 0 / 95 (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 |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 89 (0.00%) | 0 / 95 (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 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 89 (0.00%) | 0 / 95 (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 |
| Groin abscess | | | |
| subjects affected / exposed | 0 / 121 (0.00%) | 1 / 89 (1.12%) | 0 / 95 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meningitis cryptococcal | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 89 (0.00%) | 0 / 95 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic amoebiasis | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 121 (0.00%) | 0 / 89 (0.00%) | 0 / 95 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Blinded DTG + F/TDF | | |
|---|---------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 16 / 122 (13.11%) | | |
| number of deaths (all causes) | 1 | | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Laryngeal squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sinonasal papilloma | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Glottis carcinoma | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Adenocarcinoma of colon | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatocellular carcinoma | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Femoral neck fracture | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 1 / 122 (0.82%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Upper limb fracture | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Alcoholic seizure | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Death, not otherwise specified | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Eye disorders | | | |
| Rhegmatogenous retinal detachment | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 122 (0.82%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Haemorrhoids thrombosed | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Enteritis | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anal fistula | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lumbar hernia | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Irritable bowel syndrome | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|-----------------|--|--|
| Asthma | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Dermal cyst | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Suicidal ideation | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Bacterial sepsis | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anal abscess | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Covid-19 | | | |
| subjects affected / exposed | 6 / 122 (4.92%) | | |
| occurrences causally related to treatment / all | 0 / 6 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cytomegalovirus chorioretinitis | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 1 / 122 (0.82%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dengue haemorrhagic fever | | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastroenteritis | | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Mycotoxycosis | | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Orchitis | | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumocystis jirovecii pneumonia | | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia | | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pyelonephritis acute | | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Upper respiratory tract infection | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 122 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Groin abscess | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Meningitis cryptococcal | | | |
| subjects affected / exposed | 0 / 122 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatic amoebiasis | | | |
| subjects affected / exposed | 1 / 122 (0.82%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Blinded B/F/TAF | OL B/F/TAF from DTG + F/TDF | OL B/F/TAF from B/F/TAF |
|---|--------------------|-----------------------------|-------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 102 / 121 (84.30%) | 40 / 89 (44.94%) | 42 / 95 (44.21%) |
| Investigations | | | |
| Weight increased | | | |
| subjects affected / exposed | 13 / 121 (10.74%) | 6 / 89 (6.74%) | 6 / 95 (6.32%) |
| occurrences (all) | 17 | 7 | 6 |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 12 / 121 (9.92%) | 3 / 89 (3.37%) | 1 / 95 (1.05%) |
| occurrences (all) | 13 | 3 | 1 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 7 / 121 (5.79%) | 1 / 89 (1.12%) | 1 / 95 (1.05%) |
| occurrences (all) | 7 | 1 | 1 |
| Injury, poisoning and procedural complications | | | |

| | | | |
|--|---|---|---|
| Vaccination complication subjects affected / exposed occurrences (all) | 5 / 121 (4.13%) 5 | 0 / 89 (0.00%) 0 | 0 / 95 (0.00%) 0 |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 8 / 121 (6.61%) 9 | 0 / 89 (0.00%) 0 | 3 / 95 (3.16%) 3 |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) | 5 / 121 (4.13%) 5 13 / 121 (10.74%) 22 | 1 / 89 (1.12%) 1 0 / 89 (0.00%) 0 | 1 / 95 (1.05%) 1 1 / 95 (1.05%) 1 |
| General disorders and administration site conditions Influenza like illness subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) | 7 / 121 (5.79%) 7 17 / 121 (14.05%) 26 | 1 / 89 (1.12%) 1 3 / 89 (3.37%) 3 | 1 / 95 (1.05%) 1 1 / 95 (1.05%) 1 |
| Gastrointestinal disorders Gastritis subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Haemorrhoids subjects affected / exposed occurrences (all) | 8 / 121 (6.61%) 8 13 / 121 (10.74%) 15 7 / 121 (5.79%) 7 | 1 / 89 (1.12%) 1 6 / 89 (6.74%) 7 0 / 89 (0.00%) 0 | 0 / 95 (0.00%) 0 2 / 95 (2.11%) 2 1 / 95 (1.05%) 1 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 5 / 121 (4.13%) 5 | 1 / 89 (1.12%) 1 | 1 / 95 (1.05%) 1 |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|---|-------------------|----------------|----------------|
| Rash | | | |
| subjects affected / exposed | 10 / 121 (8.26%) | 0 / 89 (0.00%) | 2 / 95 (2.11%) |
| occurrences (all) | 11 | 0 | 2 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 4 / 121 (3.31%) | 0 / 89 (0.00%) | 1 / 95 (1.05%) |
| occurrences (all) | 4 | 0 | 1 |
| Infections and infestations | | | |
| Folliculitis | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 89 (0.00%) | 0 / 95 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Syphilis | | | |
| subjects affected / exposed | 8 / 121 (6.61%) | 1 / 89 (1.12%) | 2 / 95 (2.11%) |
| occurrences (all) | 9 | 1 | 2 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 18 / 121 (14.88%) | 5 / 89 (5.62%) | 7 / 95 (7.37%) |
| occurrences (all) | 25 | 7 | 10 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 22 / 121 (18.18%) | 7 / 89 (7.87%) | 7 / 95 (7.37%) |
| occurrences (all) | 30 | 8 | 7 |
| Covid-19 | | | |
| subjects affected / exposed | 48 / 121 (39.67%) | 4 / 89 (4.49%) | 5 / 95 (5.26%) |
| occurrences (all) | 56 | 4 | 5 |
| Latent syphilis | | | |
| subjects affected / exposed | 7 / 121 (5.79%) | 1 / 89 (1.12%) | 5 / 95 (5.26%) |
| occurrences (all) | 8 | 1 | 5 |
| Secondary syphilis | | | |
| subjects affected / exposed | 7 / 121 (5.79%) | 1 / 89 (1.12%) | 1 / 95 (1.05%) |
| occurrences (all) | 8 | 1 | 1 |
| Acute hepatitis C | | | |
| subjects affected / exposed | 9 / 121 (7.44%) | 0 / 89 (0.00%) | 0 / 95 (0.00%) |
| occurrences (all) | 9 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Hyperuricaemia | | | |
| subjects affected / exposed | 5 / 121 (4.13%) | 5 / 89 (5.62%) | 3 / 95 (3.16%) |
| occurrences (all) | 10 | 5 | 4 |

| | | | |
|--|----------------------|---------------------|---------------------|
| Abnormal weight gain subjects affected / exposed occurrences (all) | 4 / 121 (3.31%) 5 | 5 / 89 (5.62%) 7 | 3 / 95 (3.16%) 4 |
|--|----------------------|---------------------|---------------------|

| Non-serious adverse events | Blinded DTG + F/TDF | | |
|--|---|--|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 98 / 122 (80.33%) | | |
| Investigations Weight increased subjects affected / exposed occurrences (all) Alanine aminotransferase increased subjects affected / exposed occurrences (all) Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 12 / 122 (9.84%) 14 15 / 122 (12.30%) 19 10 / 122 (8.20%) 11 | | |
| Injury, poisoning and procedural complications Vaccination complication subjects affected / exposed occurrences (all) | 7 / 122 (5.74%) 7 | | |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 4 / 122 (3.28%) 4 | | |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) | 10 / 122 (8.20%) 12 9 / 122 (7.38%) 9 | | |
| General disorders and administration site conditions Influenza like illness subjects affected / exposed occurrences (all) | 2 / 122 (1.64%) 3 | | |

| | | | |
|---|--|--|--|
| Pyrexia subjects affected / exposed occurrences (all) | 16 / 122 (13.11%) 23 | | |
| Gastrointestinal disorders Gastritis subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Haemorrhoids subjects affected / exposed occurrences (all) | 2 / 122 (1.64%) 2 11 / 122 (9.02%) 11 2 / 122 (1.64%) 2 | | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 8 / 122 (6.56%) 8 | | |
| Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) | 9 / 122 (7.38%) 9 | | |
| Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) | 9 / 122 (7.38%) 11 | | |
| Infections and infestations Folliculitis subjects affected / exposed occurrences (all) Syphilis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection | 7 / 122 (5.74%) 8 11 / 122 (9.02%) 12 10 / 122 (8.20%) 14 | | |

| | | | |
|------------------------------------|-------------------|--|--|
| subjects affected / exposed | 20 / 122 (16.39%) | | |
| occurrences (all) | 26 | | |
| Covid-19 | | | |
| subjects affected / exposed | 52 / 122 (42.62%) | | |
| occurrences (all) | 60 | | |
| Latent syphilis | | | |
| subjects affected / exposed | 6 / 122 (4.92%) | | |
| occurrences (all) | 6 | | |
| Secondary syphilis | | | |
| subjects affected / exposed | 7 / 122 (5.74%) | | |
| occurrences (all) | 9 | | |
| Acute hepatitis C | | | |
| subjects affected / exposed | 2 / 122 (1.64%) | | |
| occurrences (all) | 2 | | |
| Metabolism and nutrition disorders | | | |
| Hyperuricaemia | | | |
| subjects affected / exposed | 6 / 122 (4.92%) | | |
| occurrences (all) | 9 | | |
| Abnormal weight gain | | | |
| subjects affected / exposed | 3 / 122 (2.46%) | | |
| occurrences (all) | 5 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|---|
| 10 April 2018 | <p>Herein is a summary of the major changes made to the original protocol dated 02 March 2018 and reflected in Amendment 1 dated 10 April 2018</p> <ul style="list-style-type: none">- Revised to include updates from ongoing bictegravir studies- Updated to include additional information in Risk/Benefit Assessment section- Update made to Biomarker Testing and Urine Samples testing- Revised to provide clarification to Management of HIV-1 Virologic Rebound- Revised to provide clarification to HBV Resistance Surveillance section <p>Specific changes contained in Amendment 1 are presented herein. New text is indicated by bold/italics.</p> <p>Study synopsis, glossary, Appendix 2 Study Procedures Table and all applicable sections are updated to align with above mentioned changes in the protocol.</p> <p>In addition, the opportunity is taken to correct the administrative, typographical or grammatical errors.</p> |
| 06 July 2018 | <p>Herein is a summary of the major changes made to Protocol Amendment 1 dated 10 April 2018 and reflected in Protocol Amendment 2 dated 06 July 2018.</p> <p>In response to FDA's Drug Safety Communication issued on May 18, 2018 for a serious finding of neural tube defect (NTD) changes have been made to the protocol sections outlined below.</p> |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/37494942>