



Clinical trial results:

A Phase 3, Randomized, Active-controlled, Double-blind study to Evaluate Efficacy and Safety of Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (D/C/F/TAF) Once Daily Fixed Dose Combination Regimen Versus a Regimen Consisting of Darunavir/Cobicistat Fixed Dose Combination Coadministered With Emtricitabine/Tenofovir Disoproxil Fumarate Fixed Dose Combination in Antiretroviral Treatment-naïve Human Immunodeficiency Virus type 1 Infected Subjects

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2015-000754-38 |
| Trial protocol | BE ES GB PL IT |
| Global end of trial date | 30 September 2020 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 16 October 2021 |
| First version publication date | 16 October 2021 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | CR107277 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02431247 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Janssen Sciences Ireland UC |
| Sponsor organisation address | Barnahely, Cork, Ireland, P43 FA46 |
| Public contact | Clinical Registry Group, Janssen Sciences Ireland UC, clinicaltrialsEU@its.jnj.com |
| Scientific contact | Clinical Registry Group, Janssen Sciences Ireland UC, clinicaltrialsEU@its.jnj.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 | 30 September 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 30 September 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to demonstrate non-inferiority in efficacy of a darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) fixed dose combination (FDC) tablet versus Darunavir/Cobicistat (DRV/COBI) FDC coadministered with Emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) FDC in human immunodeficiency virus-1 (HIV-1) infected, antiretroviral (ARV) treatment naive adult subjects, as determined by the proportion of virologic responders defined as having HIV 1 Ribonucleic Acid (RNA) less than (<) 50 copies per milliliter (copies per mL) at Week 48 (Food and Drug Administration [FDA]-defined snapshot analysis), with a maximum allowable difference of 10 percent (%).

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices (GCP) and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 06 July 2015 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Belgium: 25 |
| Country: Number of subjects enrolled | Canada: 32 |
| Country: Number of subjects enrolled | Germany: 88 |
| Country: Number of subjects enrolled | Spain: 138 |
| Country: Number of subjects enrolled | France: 51 |
| Country: Number of subjects enrolled | United Kingdom: 14 |
| Country: Number of subjects enrolled | Italy: 80 |
| Country: Number of subjects enrolled | Poland: 78 |
| Country: Number of subjects enrolled | Russian Federation: 86 |
| Country: Number of subjects enrolled | United States: 133 |
| Worldwide total number of subjects | 725 |
| EEA total number of subjects | 460 |

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) | 724 |
| From 65 to 84 years | 1 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 725 subjects (362 to D/C/F/TAF group and 363 in control group). 296 subjects in D/C/F/TAF group and 289 subjects in control group completed the study and 66 subject in D/C/F/TAF group and 74 subjects in control group discontinued the study.

Period 1

| | |
|------------------------------|--|
| Period 1 title | BL to EOE-Test and BL to Switch- Control |
| 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 | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) |

Arm description:

Subjects received a single oral tablet containing darunavir (DRV) 800 milligram (mg)/ cobicistat (COBI) 150 mg/ emtricitabine (FTC) 200 mg/ tenofovir alafenamide (TAF) 10 mg (D/C/F/TAF fixed dose combination [FDC]) once daily along with DRV/COBI FDC-matching placebo and FTC/tenofovir disoproxil fumarate (TDF) FDC-matching placebo tablets once daily up to Week 48 analysis unblinding visit (that is, after last subject has reached Week 48). After Week 48 analysis unblinding visit, all subjects received D/C/F/TAF treatment up to Week 96 during the open-label, single-group treatment phase. After Week 96, subjects were given the opportunity to continue D/C/F/TAF treatment during an extension phase until the D/C/F/TAF FDC tablet became commercially available.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Darunavir 800 mg/Cobicistat 150 mg/Emtricitabine 200 mg/Tenofovir Alafenamide 10 mg (D/C/F/TAF) FDC |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received a single oral tablet of D/C/F/TAF 800/150/200/10 mg FDC once daily.

| | |
|--|------------------------------|
| Investigational medicinal product name | FTC/TDF FDC-matching Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subject received a single oral placebo tablet matching to FTC/TDF FDC once daily.

| | |
|--|-------------------------------|
| Investigational medicinal product name | DRV/COBI FDC-matching Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subject received a single oral placebo tablet matching to DRV/COBI FDC once daily.

| | |
|------------------|--|
| Arm title | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) |
|------------------|--|

Arm description:

Subjects received DRV 800 mg/COBI 150 mg FDC and FTC 200 mg/TDF 300 mg FDC along with D/C/F/TAF FDC-matching placebo tablet once daily up to Week 48 analysis unblinding visit (that is, after last subject has reached Week 48).

| | |
|--|--------------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | D/C/F/TAF FDC-matching Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subject received a single oral placebo tablet matching to D/C/F/TAF FDC once daily.

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

Dosage and administration details:

Subject received a single oral tablet of FTC/TDF FDC once daily.

| | |
|--|--------------|
| Investigational medicinal product name | DRV/COBI FDC |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subject received a single oral tablet of DRV/COBI FDC once daily.

| Number of subjects in period 1 | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) |
|---------------------------------------|---|--|
| Started | 362 | 363 |
| Completed | 296 | 322 |
| Not completed | 66 | 41 |
| Adverse event, serious fatal | - | 1 |
| Consent withdrawn by subject | 14 | 9 |
| Physician decision | 9 | 4 |
| Adverse event, non-fatal | 12 | 16 |
| Pregnancy | 1 | 1 |
| Non-compliance with study drug | 2 | - |
| Unspecified | 11 | 2 |
| Lost to follow-up | 17 | 8 |

Period 2

| | |
|------------------------------|---------------------------------|
| Period 2 title | Switch to D/C/F/TAF (until EOE) |
| Is this the baseline period? | No |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------|---------------------|
| Arm title | Switch to D/C/F/TAF |
|------------------|---------------------|

Arm description:

After Week 48 analysis unblinding visit, subjects earlier receiving treatment with DRV/COBI+ FTC/TDF (Control) switched to D/C/F/TAF treatment and continued for up to Week 96 during open-label, single-group treatment phase. After Week 96, subjects were given the opportunity to continue D/C/F/TAF treatment until the D/C/F/TAF FDC tablet became commercially available.

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

Dosage and administration details:

Subjects received a single oral tablet of D/C/F/TAF FDC once daily.

| Number of subjects in period 2^[1] | Switch to D/C/F/TAF |
|---|---------------------|
| Started | 322 |
| Completed | 289 |
| Not completed | 33 |
| Adverse event, serious fatal | 1 |
| Consent withdrawn by subject | 10 |
| Physician decision | 1 |
| Adverse event, non-fatal | 5 |
| Unspecified | 4 |
| Lost to follow-up | 12 |

Notes:

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

Justification: Out of 363 subjects in the DRV/COBI+ FTC/TDF (Control) group, 322 subjects switched to D/C/F/TAF treatment after Week 48 or unblinding.

Baseline characteristics

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) |
|-----------------------|--|

Reporting group description:

Subjects received a single oral tablet containing darunavir (DRV) 800 milligram (mg)/ cobicistat (COBI) 150 mg/ emtricitabine (FTC) 200 mg/ tenofovir alafenamide (TAF) 10 mg (D/C/F/TAF fixed dose combination [FDC]) once daily along with DRV/COBI FDC-matching placebo and FTC/tenofovir disoproxil fumarate (TDF) FDC-matching placebo tablets once daily up to Week 48 analysis unblinding visit (that is, after last subject has reached Week 48). After Week 48 analysis unblinding visit, all subjects received D/C/F/TAF treatment up to Week 96 during the open-label, single-group treatment phase. After Week 96, subjects were given the opportunity to continue D/C/F/TAF treatment during an extension phase until the D/C/F/TAF FDC tablet became commercially available.

| | |
|-----------------------|--|
| Reporting group title | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) |
|-----------------------|--|

Reporting group description:

Subjects received DRV 800 mg/COBI 150 mg FDC and FTC 200 mg/TDF 300 mg FDC along with D/C/F/TAF FDC-matching placebo tablet once daily up to Week 48 analysis unblinding visit (that is, after last subject has reached Week 48).

| Reporting group values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) | Total |
|---|---|--|-------|
| Number of subjects | 362 | 363 | 725 |
| Title for AgeCategorical Units: subjects | | | |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 362 | 362 | 724 |
| From 65 to 84 years | 0 | 1 | 1 |
| 85 years and over | 0 | 0 | 0 |
| Title for AgeContinuous Units: years | | | |
| median | 34 | 34 | |
| full range (min-max) | 19 to 61 | 18 to 71 | - |
| Title for Gender Units: subjects | | | |
| Female | 44 | 41 | 85 |
| Male | 318 | 322 | 640 |

End points

End points reporting groups

| | |
|-----------------------|--|
| Reporting group title | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) |
|-----------------------|--|

Reporting group description:

Subjects received a single oral tablet containing darunavir (DRV) 800 milligram (mg)/ cobicistat (COBI) 150 mg/ emtricitabine (FTC) 200 mg/ tenofovir alafenamide (TAF) 10 mg (D/C/F/TAF fixed dose combination [FDC]) once daily along with DRV/COBI FDC-matching placebo and FTC/tenofovir disoproxil fumarate (TDF) FDC-matching placebo tablets once daily up to Week 48 analysis unblinding visit (that is, after last subject has reached Week 48). After Week 48 analysis unblinding visit, all subjects received D/C/F/TAF treatment up to Week 96 during the open-label, single-group treatment phase. After Week 96, subjects were given the opportunity to continue D/C/F/TAF treatment during an extension phase until the D/C/F/TAF FDC tablet became commercially available.

| | |
|-----------------------|--|
| Reporting group title | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) |
|-----------------------|--|

Reporting group description:

Subjects received DRV 800 mg/COBI 150 mg FDC and FTC 200 mg/TDF 300 mg FDC along with D/C/F/TAF FDC-matching placebo tablet once daily up to Week 48 analysis unblinding visit (that is, after last subject has reached Week 48).

| | |
|-----------------------|---------------------|
| Reporting group title | Switch to D/C/F/TAF |
|-----------------------|---------------------|

Reporting group description:

After Week 48 analysis unblinding visit, subjects earlier receiving treatment with DRV/COBI+ FTC/TDF (Control) switched to D/C/F/TAF treatment and continued for up to Week 96 during open-label, single-group treatment phase. After Week 96, subjects were given the opportunity to continue D/C/F/TAF treatment until the D/C/F/TAF FDC tablet became commercially available.

| | |
|----------------------------|-------------------------------------|
| Subject analysis set title | Darunavir 800 mg (D/C/F/TAF [Test]) |
|----------------------------|-------------------------------------|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Intention-to-treat |
|---------------------------|--------------------|

Subject analysis set description:

Subjects received DRV 800 mg along with COBI 150 mg, FTC 200 mg, TAF 10 mg as a (D/C/F/TAF) FDC oral tablet once daily along with DRV/COBI FDC matching placebo and FTC/TDF FDC-matching placebo tablets once daily up to Week 48.

| | |
|----------------------------|--|
| Subject analysis set title | Tenofovir Alafenamide 10 mg (D/C/F/TAF [Test]) |
|----------------------------|--|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Intention-to-treat |
|---------------------------|--------------------|

Subject analysis set description:

Subjects received TAF 10 mg along with DRV 800 mg, COBI 150 mg, FTC 200 mg as a (D/C/F/TAF) FDC oral tablet once daily along with DRV/COBI FDC-matching placebo and FTC/TDF FDC-matching placebo tablets once daily up to Week 48.

Primary: Percentage of Subjects With Human Immunodeficiency Virus (HIV)-1 Ribonucleic Acid (RNA) less than (<) 50 Copies per Milliliter (Copies per mL) (Virologic Response) at Week 48 Defined by Food and Drug Administration (FDA) Snapshot Approach

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Human Immunodeficiency Virus (HIV)-1 Ribonucleic Acid (RNA) less than (<) 50 Copies per Milliliter (Copies per mL) (Virologic Response) at Week 48 Defined by Food and Drug Administration (FDA) Snapshot Approach |
|-----------------|--|

End point description:

Percentage of subjects with a HIV-1 RNA < 50 copies per mL were assessed using FDA snapshot approach which defines a subject'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 snapshot approach classified subjects into 3 outcome categories: 1) virologic success (HIV RNA < 20/50/200 copies per mL at Week 48), 2) virologic failure (HIV RNA greater than or equal to [\geq] 20/50/200 copies per mL at Week 48), 3) no viral load data in the Week 48 visit window (discontinued due to adverse event/death/other reason). The missing HIV-1 RNA is considered as non-response. The intent-to-treat (ITT) analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here N (number of subjects analyzed) refers to 363 for test group and 363 for control group.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

At Week 48

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) | | |
|----------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 362 | 363 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 91.4 (88.1 to 94.1) | 88.4 (84.7 to 91.5) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) |
| Number of subjects included in analysis | 725 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 ^[1] |
| Method | Mantel-Haenszel |
| Parameter estimate | Difference in percentage |
| Point estimate | 2.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.6 |
| upper limit | 7.1 |

Notes:

[1] - One-sided p-value for non-inferiority of Test versus Control arm. The non-inferiority margin is 10%.

Secondary: Percentage of Subjects With HIV-1 RNA <20 and 200 Copies per mL at Week 48 and 96 Defined by FDA Snapshot Approach

| | |
|-----------------|---|
| End point title | Percentage of Subjects With HIV-1 RNA <20 and 200 Copies per mL at Week 48 and 96 Defined by FDA Snapshot Approach |
|-----------------|---|

End point description:

Percentage of subjects with HIV-1 RNA < 20/200 copies per mL using FDA snapshot approach were reported. The snapshot approach classified subjects into 3 outcome categories: 1) virologic success (HIV RNA < 20/50/200 copies per mL at Week 48 and 96), 2) virologic failure (HIV RNA ≥ 20/50/200 copies per mL at Week 48 and 96), 3) no viral load data in the Week 48 and 96 visit window (discontinued due to adverse event/death/other reason). The missing HIV-1 RNA is considered as non-response. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint. Here, 99999 refers that subjects received treatment from baseline till Week 48/Switch in control arm and from switch till Week 96 in Switch to D/C/F/TAF arm. Therefore, Week 96 and Week 48 data was not collected for both arms at respective timepoints.

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

End point timeframe:

At Weeks 48 and 96

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) | |
|----------------------------------|---|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 362 | 291 | 363 | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| At 48 week: <20 Copies per mL | 82.6 (78.3 to 86.4) | 99999 (99999 to 99999) | 79.3 (74.8 to 83.4) | |
| At 48 week: <200 Copies per mL | 92.8 (89.7 to 95.3) | 99999 (99999 to 99999) | 90.6 (87.2 to 93.4) | |
| At 96 week: <20 Copies per mL | 76.2 (71.5 to 80.5) | 83.5 (78.7 to 87.6) | 99999 (99999 to 99999) | |
| At 96 week: <200 Copies per mL | 86.2 (82.2 to 89.6) | 96.9 (94.2 to 98.6) | 99999 (99999 to 99999) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with HIV-1 RNA < 20, 50, and 200 Copies per mL at Week 48 and 96 Defined by the Time to Loss of Virologic Response (TLOVR) Algorithm

| | |
|-----------------|---|
| End point title | Percentage of Subjects with HIV-1 RNA < 20, 50, and 200 Copies per mL at Week 48 and 96 Defined by the Time to Loss of Virologic Response (TLOVR) Algorithm |
|-----------------|---|

End point description:

Percentage of subjects with HIV-1 RNA <20, 50, and 200 copies per mL at Weeks 48 and 96 based on TLOVR algorithm were assessed. TLOVR requires sustained HIV-1 RNA < 50 copies per mL; confirmed HIV-1 RNA ≥ 50 copies per mL is considered as non-response (rebound); subject is considered non-responder after permanent discontinuation. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint. Here, 99999 refers that subjects received treatment from baseline till Week 48/Switch in control arm and from switch till Week 96 in Switch to D/C/F/TAF arm. Therefore, Week 96 and Week 48 data was not collected for both arms at respective timepoints.

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

End point timeframe:

At Week 48 and 96

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) | |
|----------------------------------|---|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 362 | 291 | 363 | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| At Week 48: < 20 Copies per mL | 82.6 (78.3 to 86.4) | 99999 (99999 to 99999) | 79.9 (75.4 to 83.9) | |
| At Week 48: <50 Copies per mL | 91.2 (87.8 to 93.9) | 99999 (99999 to 99999) | 88.7 (85.0 to 91.8) | |
| At Week 48: <200 Copies per mL | 93.1 (90.0 to 95.5) | 99999 (99999 to 99999) | 91.7 (88.4 to 94.4) | |
| At Week 96: <20 Copies per mL | 73.2 (68.3 to 77.7) | 78.4 (73.2 to 82.9) | 99999 (99999 to 99999) | |
| At Week 96: <50 Copies per mL | 85.1 (81.0 to 88.6) | 93.8 (90.4 to 96.3) | 99999 (99999 to 99999) | |
| At Week 96: <200 Copies per mL | 86.7 (82.8 to 90.1) | 96.9 (94.2 to 98.6) | 99999 (99999 to 99999) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in log10 HIV-1 RNA Levels at Week 48

| | |
|--|---|
| End point title | Change From Baseline in log10 HIV-1 RNA Levels at Week 48 |
| End point description: | |
| Change from baseline in log10 HIV-1 RNA levels were reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Based on not completed (NC) equal to (=) failure (F) analysis with values after discontinuation imputed with the baseline value. Other (intermittent) missing values are imputed using last observation carried forward (LOCF). | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Week 48 | |

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) | | |
|--------------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 362 | 363 | | |
| Units: log10 HIV-1 RNA copies per mL | | | | |
| least squares mean (standard error) | -2.95 (± 0.044) | -2.91 (± 0.044) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) |
| Number of subjects included in analysis | 725 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.437 |
| Method | ANCOVA |
| Parameter estimate | Least square mean difference |
| Point estimate | -0.05 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.171 |
| upper limit | 0.074 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.063 |

Secondary: Change From Baseline in Cluster of Differentiation-4 (CD4+) Cell Count at Week 48

| | |
|------------------------|--|
| End point title | Change From Baseline in Cluster of Differentiation-4 (CD4+) Cell Count at Week 48 |
| End point description: | The immunologic change was determined by changes in Cluster of CD4+ cell count. Change from baseline in CD4+ cell count at Week 48 were assessed. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Based on NC = F analysis with values after discontinuation imputed with the baseline value. Other (intermittent) missing values are imputed using LOCF. |
| End point type | Secondary |
| End point timeframe: | Baseline and Week 48 |

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) | | |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 362 | 363 | | |
| Units: Cells per millimeter cube | | | | |

| | | | | |
|-------------------------------------|-------------------|-------------------|--|--|
| (cells/mm ³) | | | | |
| least squares mean (standard error) | 190.49 (± 10.472) | 172.01 (± 10.458) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) |
| Number of subjects included in analysis | 725 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.213 |
| Method | ANCOVA |
| Parameter estimate | LS mean difference |
| Point estimate | 18.48 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10.595 |
| upper limit | 47.55 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 14.808 |

Secondary: Change From Baseline in Serum Creatinine at Week 48

| | |
|------------------------|--|
| End point title | Change From Baseline in Serum Creatinine at Week 48 |
| End point description: | Change from baseline in serum creatinine at Week 48 was reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint. |
| End point type | Secondary |
| End point timeframe: | Baseline and Week 48 |

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) | | |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 340 | 330 | | |
| Units: milligram per deciliter (mg/dL) | | | | |
| least squares mean (standard error) | 0.05 (± 0.006) | 0.09 (± 0.006) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) |
| Number of subjects included in analysis | 670 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | LS mean difference |
| Point estimate | -0.04 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.05 |
| upper limit | -0.02 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.008 |

Secondary: Change From Baseline in Estimated Glomerular Filtration Rate Based on Serum Creatinine (eGFRcr) by Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) Formula at Week 48

| | |
|-----------------|---|
| End point title | Change From Baseline in Estimated Glomerular Filtration Rate Based on Serum Creatinine (eGFRcr) by Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) Formula at Week 48 |
|-----------------|---|

End point description:

Change from baseline in eGFRcr was calculated using the CKD-EPI equation as per which Stage 1 (normal or high GFR [≥ 90 mL/min]); Stage 2 (Mild CKD [60 to 90 mL/min]); Stage 3 (Moderate CKD [30 to 59 mL/min]); Stage 4 (Severe CKD [15 to 29 mL/min]); Stage 5 (End Stage CKD [< 15 mL/min]). The eGFRcr was assessed by calculating serum creatinine (Scr) using the equation: eGFRcr milliliter per minute per 1.72 meter square (mL/min/1.73m²) = $144 \times (\text{Scr}/0.7)^{-0.329} \times 0.993^{\text{age}}$ (Scr = ≤ 0.7 mg/dL) and eGFRcr mL/min/1.73m² = $144 \times (\text{Scr}/0.7)^{-1.209} \times 0.993^{\text{age}}$ (Scr > 0.7 mg/dL) for female subjects and eGFRcr mL/min/1.73m² = $141 \times (\text{Scr}/0.9)^{-0.411} \times 0.993^{\text{age}}$ (Scr = ≤ 0.9 mg/dL) and eGFRcr mL/min/1.73m² = $141 \times (\text{Scr}/0.9)^{-1.209} \times 0.993^{\text{age}}$ (Scr > 0.9 mg/dL) for male subjects. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Week 48 | |

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) | | |
|-------------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 340 | 330 | | |
| Units: mL/min/1.73 m ² | | | | |
| least squares mean (standard error) | -6.04 (± 0.551) | -9.16 (± 0.559) | | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) |
| Number of subjects included in analysis | 670 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | LS mean difference |
| Point estimate | 3.12 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.57 |
| upper limit | 4.66 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.786 |

Secondary: Change From Baseline in Estimated Glomerular Filtration Rate Based on Serum Creatinine by (Cockcroft-Gault Formula) at Week 48

| | |
|--|--|
| End point title | Change From Baseline in Estimated Glomerular Filtration Rate Based on Serum Creatinine by (Cockcroft-Gault Formula) at Week 48 |
| End point description: | |
| Change from baseline in eGFRcr by (cockcroft-gault formula) was reported. The eGFRcr was assessed by calculated creatinine clearance (CrCl) using the Cockcroft-Gault formula, and was assessed using CrCl [mL/min] = (140 – A) * W / (72 * C) * R. Where A is age at sample date [years], W is body weight at specific visit (kilogram [kg]), C is the serum concentration of creatinine [mg/dL], R=1 if the subject is male and = 0.85 if female. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Week 48 | |

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) | | |
|---------------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 340 | 330 | | |
| Units: milliliter per minute (mL/min) | | | | |
| least squares mean (standard error) | -5.16 (± 0.790) | -11.20 (± 0.802) | | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) |
| Number of subjects included in analysis | 670 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | LS mean difference |
| Point estimate | 6.04 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 3.83 |
| upper limit | 8.25 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.126 |

Secondary: Change From Baseline in Estimated Glomerular Filtration Rate Based on Serum Cystatin C (eGFRcyst) by CKD-EPI Formula at Week 48

| | |
|-----------------|---|
| End point title | Change From Baseline in Estimated Glomerular Filtration Rate Based on Serum Cystatin C (eGFRcyst) by CKD-EPI Formula at Week 48 |
|-----------------|---|

End point description:

Change from baseline in eGFRcyst was calculated using the CKD-EPI equation as per which Stage 1 (normal or high GFR) ≥ 90 indicates normal kidney function; Stage 2 (Mild CKD): 60 to 89 mL/min indicates mildly reduced kidney function; Stage 3 (Moderate CKD): 30 to 59 mL/min indicates moderately reduced kidney function; Stage 4 (Severe CKD): 15 to 29 mL/min indicates severely reduced kidney function; Stage 5 (End Stage of CKD): <15 mL/min indicate very severe or end stage kidney failure. The eGFRcyst was assessed by calculated serum cystatin C (Scyst) using the equation: $\text{eGFRcyst mL/min}/1.73\text{m}^2 = 133 \times (\text{Scyst}/0.8)^{-0.499} \times 0.996^{\text{age}} [\times 0.932 \text{ if female}]$ ($\text{Scyst} \leq 0.8$ mg/L) and $\text{eGFRcr mL/min}/1.73\text{m}^2 = 133 \times (\text{Scyst}/0.8)^{-1.328} \times 0.996^{\text{age}} [\times 0.932 \text{ if male}]$ ($\text{Scyst} > 0.8$ mg/L). The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects

evaluated for this endpoint.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Week 48 | |

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) | | |
|-------------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 337 | 329 | | |
| Units: mL/min/1.73 m ² | | | | |
| least squares mean (standard error) | 5.32 (± 0.525) | 2.92 (± 0.532) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) |
| Number of subjects included in analysis | 666 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.001 |
| Method | ANCOVA |
| Parameter estimate | LS mean difference |
| Point estimate | 2.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.93 |
| upper limit | 3.87 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.747 |

Secondary: Percentage of Subjects With Grade 3 and 4 Adverse Events (AEs), Serious Adverse Events (SAEs), and Premature Discontinuations due to Adverse Events Through Week 48

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Grade 3 and 4 Adverse Events (AEs), Serious Adverse Events (SAEs), and Premature Discontinuations due to Adverse Events Through Week 48 |
|-----------------|---|

End point description:

AE is any untoward medical occurrence in subject who received study drug without regard to possibility of causal relationship. Events with Grade 3 or higher (3=Severe; 4=life-threatening; 5=fatal) are events that significantly interrupt usual daily activity, require systemic drug therapy/other treatment and are, in many situations, considered unacceptable or intolerable events. SAE is any adverse event (AE) that results in: death, persistent or significant disability/incapacity, requires inpatient hospitalization or

prolongation of existing hospitalization, is life-threatening experience, is a congenital anomaly/birth defect and may jeopardize subject and/or may require medical or surgical intervention to prevent one of the outcomes listed above. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Up to Week 48 | |

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) | | |
|---------------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 362 | 363 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Grade 3 AEs | 4.7 | 4.4 | | |
| Grade 4 AEs | 0.6 | 1.7 | | |
| SAEs | 4.7 | 5.8 | | |
| Premature discontinuations due to AEs | 1.9 | 4.4 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Urine Protein to Creatinine Ratio (UPCR) at Week 48

| | |
|-----------------|---|
| End point title | Change From Baseline in Urine Protein to Creatinine Ratio (UPCR) at Week 48 |
|-----------------|---|

End point description:

Change from baseline in UPCR at Week 48 was reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Week 48 | |

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) | | |
|----------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 336 | 325 | | |
| Units: milligram per gram (mg/g) | | | | |

| | | | | |
|-------------------------------|--------------------------|---------------------------|--|--|
| median (full range (min-max)) | -15.72 (-748.1 to 254.2) | -10.53 (-903.0 to 1546.1) | | |
|-------------------------------|--------------------------|---------------------------|--|--|

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) |
| Number of subjects included in analysis | 661 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.033 |
| Method | Wilcoxon rank sum test |

Secondary: Change From Baseline in Urine Albumin to Creatinine Ratio (UACR) at Week 48

| | |
|--|---|
| End point title | Change From Baseline in Urine Albumin to Creatinine Ratio (UACR) at Week 48 |
| End point description: Change from baseline in UACR at Week 48 was reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint. | |
| End point type | Secondary |
| End point timeframe: Baseline and Week 48 | |

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) | | |
|-------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 338 | 327 | | |
| Units: mg/g | | | | |
| median (full range (min-max)) | -0.58 (-226.5 to 143.8) | -0.15 (-640.4 to 969.6) | | |

Statistical analyses

| | |
|-----------------------------------|---|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) |

| | |
|---|------------------------|
| Number of subjects included in analysis | 665 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.033 |
| Method | Wilcoxon rank sum test |

Secondary: Change From Baseline in Urine Retinol Binding Protein To Creatinine Ratio (URBPCR) at Week 48

| | |
|-----------------|---|
| End point title | Change From Baseline in Urine Retinol Binding Protein To Creatinine Ratio (URBPCR) at Week 48 |
|-----------------|---|

End point description:

Change from baseline in URBPCR at Week 48 was reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint.

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

End point timeframe:

Baseline and Week 48

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) | | |
|-----------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 334 | 324 | | |
| Units: microgram per gram (mcg/g) | | | | |
| median (full range (min-max)) | 7.00 (-1555.7 to 5183.8) | 35.02 (-700.7 to 30350.2) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) |
| Number of subjects included in analysis | 658 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | Wilcoxon rank sum test |

Secondary: Change From Baseline in Urine Beta-2 Microglobulin to Creatinine Ratio (UB2MGCR) at Week 48

| | |
|-----------------|---|
| End point title | Change From Baseline in Urine Beta-2 Microglobulin to Creatinine Ratio (UB2MGCR) at Week 48 |
|-----------------|---|

End point description:

Change from baseline in UB2MGCR at Week 48 was reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Week 48 | |

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) | | |
|-------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 331 | 320 | | |
| Units: mcg/g | | | | |
| median (full range (min-max)) | -30.42 (- 11818.6 to 3452.0) | 18.36 (-2440.5 to 90832.0) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) |
| Number of subjects included in analysis | 651 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | Wilcoxon rank sum test |

Secondary: Percent Change From Baseline in Urine Fractional Excretion of Phosphate (FEPO4) at Week 48

| | |
|-----------------|---|
| End point title | Percent Change From Baseline in Urine Fractional Excretion of Phosphate (FEPO4) at Week 48 |
|-----------------|---|

End point description:

Percent change from baseline in FEPO4 at Week 48 was reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Week 48 | |

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) | | |
|--------------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 339 | 329 | | |
| Units: Percent change in urine FEP04 | | | | |
| median (full range (min-max)) | 16.00 (-87.3 to 1756.6) | 22.55 (-90.1 to 1720.7) | | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) |
| Number of subjects included in analysis | 668 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.147 |
| Method | Wilcoxon rank sum test |

Secondary: Area Under the Plasma Concentration-Time Curve From Time of Administration to 24 Hours Post-dose (AUC0-24h) of Darunavir

| | |
|-----------------|--|
| End point title | Area Under the Plasma Concentration-Time Curve From Time of Administration to 24 Hours Post-dose (AUC0-24h) of Darunavir |
|-----------------|--|

End point description:

AUC (0-24) is the area under the plasma concentration-time curve from time zero to 24 hours post-dose. Pharmacokinetic(PK) analysis set: all subjects who were randomized, received at least 1 dose of study drug and plasma concentration data for analytes of interest were available. PK data of DRV was analyzed only for test arm as per planned analyses. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint.

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

End point timeframe:

0 to 24 hours post dose

| End point values | Darunavir 800 mg (D/C/F/TAF [Test]) | | | |
|---|-------------------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 355 | | | |
| Units: hour*nanogram per milliliter (h*ng/mL) | | | | |
| arithmetic mean (standard deviation) | 87909.3282 (± 20232.09905) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Predose (Trough) Plasma Concentration (C0h) of Darunavir

| | |
|-----------------|--|
| End point title | Predose (Trough) Plasma Concentration (C0h) of Darunavir |
|-----------------|--|

End point description:

C0h is defined as the predose (trough) plasma concentration or concentration just prior to study drug administration. PK analysis set: all subjects who were randomized, received at least 1 dose of study drug and plasma concentration data for analytes of interest were available. PK data of DRV was analyzed only for test arm as per planned analyses. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint.

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

End point timeframe:

30 minutes to 4 hours postdose at Weeks 2, 4, 12, 24 and 48 and at 2 timepoints with at least 2.5 hours in between sampling at Week 8 and 36 (first sample between 1 and 4 hours postdose)

| | | | | |
|--|-------------------------------------|--|--|--|
| End point values | Darunavir 800 mg (D/C/F/TAF [Test]) | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 355 | | | |
| Units: nanogram per milliliter (ng/mL) | | | | |
| arithmetic mean (standard deviation) | 1898.9100 (± 758.83837) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration Time Curve Across the Dosing Interval (AUCtau) of Tenofovir Alafenamide

| | |
|-----------------|---|
| End point title | Area Under the Plasma Concentration Time Curve Across the Dosing Interval (AUCtau) of Tenofovir Alafenamide |
|-----------------|---|

End point description:

The AUCtau is the measure of the plasma drug concentration from time zero to end of dosing interval. It is used to characterize drug absorption. PK analysis set: all subjects who were randomized, received at least 1 dose of study drug and plasma concentration data for analytes of interest were available. PK data of TAF was analyzed only for test arm as per planned analyses. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint.

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

End point timeframe:

30 minutes to 4 hours postdose at Weeks 2, 4, 12, 24 and 48 and at 2 timepoints with at least 2.5 hours in between sampling at Week 8 and 36 (first sample between 1 and 4 hours postdose)

| | | | | |
|--------------------------------------|--|--|--|--|
| End point values | Tenofovir Alafenamide 10 mg (D/C/F/TAF [Test]) | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 355 | | | |
| Units: h*ng/mL | | | | |
| arithmetic mean (standard deviation) | 132.3117 (\pm 40.87742) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations 2 hours After Dosing (C0-2h) of Tenofovir Alafenamide

| | |
|-----------------|---|
| End point title | Plasma Concentrations 2 hours After Dosing (C0-2h) of Tenofovir Alafenamide |
|-----------------|---|

End point description:

C0-2h is defined as the plasma concentrations 2 hours after dosing. PK analysis set: all subjects who were randomized, received at least 1 dose of study drug and plasma concentration data for analytes of interest were available. PK data of TAF was analyzed only for test arm as per planned analyses. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint.

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

End point timeframe:

0 to 2 hours post dose

| | | | | |
|--------------------------------------|--|--|--|--|
| End point values | Tenofovir Alafenamide 10 mg (D/C/F/TAF [Test]) | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 355 | | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | 11.9785 (\pm 11.86104) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Hip and Spine Bone Mineral Density (BMD)

| | |
|-----------------|--|
| End point title | Percent Change From Baseline in Hip and Spine Bone Mineral |
|-----------------|--|

End point description:

The BMD is the amount of mineral in gram per square centimeter of bone, which was assessed by dual energy x-ray absorptiometry (DEXA) scan. Positive values are "best values" and negative values are "worst values" of change. Percent change from baseline in hip and spine BMD was assessed. Bone investigation substudy (BIS) analysis set included all subjects who were randomized, received at least 1 dose of study drug in study and had at least one post-baseline value for either biomarker/BMD data. Here, n (number analyzed) signifies subjects analyzed for this endpoint at specified timepoints.

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

End point timeframe:

Baseline, Week 24 and 48

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) | | |
|-------------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 113 | 99 | | |
| Units: Percent change | | | | |
| least squares mean (standard error) | | | | |
| Hip region BMD (Week 24) n= 97, 82 | 0.29 (± 0.248) | -1.66 (± 0.269) | | |
| Spine region BMD (Week 24) n=96, 82 | -1.34 (± 0.285) | -3.43 (± 0.309) | | |
| Hip region BMD (Week 48) n=96, 85 | 0.17 (± 0.322) | -2.69 (± 0.342) | | |
| Spine region BMD (Week 48) n=96, 85 | -0.68 (± 0.402) | -2.38 (± 0.428) | | |

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

Hip region BMD (Week 24)

| | |
|---|---|
| Comparison groups | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) |
| Number of subjects included in analysis | 212 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | LS mean difference |
| Point estimate | 1.95 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.227 |
| upper limit | 2.678 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.368 |

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 2 |
| Statistical analysis description: Hip region BMD (Week 48) | |
| Comparison groups | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) |
| Number of subjects included in analysis | 212 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | LS mean difference |
| Point estimate | 2.86 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.934 |
| upper limit | 3.791 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.47 |

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 3 |
| Statistical analysis description: Spine region BMD (Week 24) | |
| Comparison groups | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) |
| Number of subjects included in analysis | 212 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | LS mean difference |
| Point estimate | 2.09 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.259 |
| upper limit | 2.919 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.421 |

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 4 |
|-----------------------------------|------------------------|

Statistical analysis description:

Spine region BMD (Week 48)

| | |
|---|---|
| Comparison groups | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) v DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) |
| Number of subjects included in analysis | 212 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.004 |
| Method | ANCOVA |
| Parameter estimate | LS mean difference |
| Point estimate | 1.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.539 |
| upper limit | 2.858 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.588 |

Secondary: Change From Baseline in BMD T-score of Hip and Spine

| | |
|-----------------|--|
| End point title | Change From Baseline in BMD T-score of Hip and Spine |
|-----------------|--|

End point description:

BMD status was assessed using BMD T-scores; normal bone status was defined by a BMD T-score ≥ -1 , osteopenia by a T-score ≥ -2.5 to < -1.0 , and osteoporosis by a T-score < -2.5 . BIS analysis set included all subjects who were randomized, received at least 1 dose of study drug in study and had at least one post-baseline value for either biomarker/BMD data. Here, n (number analyzed) signifies subjects analyzed for this endpoint at specified timepoints.

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

End point timeframe:

Baseline, Week 24 and 48

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) | | |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 113 | 99 | | |
| Units: BMD T-score | | | | |
| arithmetic mean (standard error) | | | | |
| Hip region BMD T-score (Week 24) n= 97, 82 | 0.019 (\pm 0.0180) | -0.109 (\pm 0.0157) | | |
| Spine region BMD T-score (Week 24) n= 96, 82 | -0.121 (\pm 0.0259) | -0.322 (\pm 0.0307) | | |
| Hip region BMD T-score (Week 48) n= 96, 85 | 0.015 (\pm 0.0213) | -0.177 (\pm 0.0225) | | |
| Spine region BMD T-score (Week 48) n= 96, 85 | -0.061 (\pm 0.0390) | -0.225 (\pm 0.0386) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Alkaline Phosphatase (ALP) Levels at Week 24 and 48

| | |
|-----------------|---|
| End point title | Change From Baseline in Alkaline Phosphatase (ALP) Levels at Week 24 and 48 |
|-----------------|---|

End point description:

Change from baseline in ALP at Weeks 24 and 48 were reported. BIS analysis set included all subjects who were randomized, received at least 1 dose of study drug in study and had at least one post-baseline value for either biomarker/BMD data. Here, n (number analyzed) signifies subjects analyzed for this endpoint at specified timepoints.

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

End point timeframe:

Baseline, Week 24 and 48

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) | | |
|----------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 113 | 99 | | |
| Units: Units per liter (U/L) | | | | |
| arithmetic mean (standard error) | | | | |
| Week 24: n=103, 88 | -3.2 (\pm 1.17) | 12.0 (\pm 1.74) | | |
| Week 48: n=97, 85 | -1.1 (\pm 1.29) | 15.1 (\pm 2.00) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Levels of Serum Procollagen 1 N-Terminal Propeptide (P1NP) at Week 24 and 48

| | |
|-----------------|--|
| End point title | Change From Baseline in Levels of Serum Procollagen 1 N-Terminal Propeptide (P1NP) at Week 24 and 48 |
|-----------------|--|

End point description:

Change from baseline in serum P1NP at Weeks 24 and 48 were reported. BIS analysis set included all subjects who were randomized, received at least 1 dose of study drug in study and had at least one post-baseline value for either biomarker/BMD data. Here, n (number analyzed) signifies subjects analyzed for this endpoint at specified timepoints.

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

End point timeframe:

Baseline, Week 24 and 48

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) | | |
|------------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 113 | 99 | | |
| Units: microgram per liter (mcg/L) | | | | |
| arithmetic mean (standard error) | | | | |
| Week 24: n= 101, 95 | 1.892 (± 1.3754) | 24.679 (± 2.0956) | | |
| Week 48: n= 96, 84 | 0.065 (± 1.6428) | 24.251 (± 2.6337) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Levels of Serum Collagen Type 1 Beta Carboxy Telopeptide (CTX) at Week 24 and 48

| | |
|-----------------|--|
| End point title | Change From Baseline in Levels of Serum Collagen Type 1 Beta Carboxy Telopeptide (CTX) at Week 24 and 48 |
|-----------------|--|

End point description:

Change from baseline in serum CTX at Week 24 and 48 were reported. BIS analysis set included all subjects who were randomized, received at least 1 dose of study drug in study and had at least one post-baseline value for either biomarker/BMD data. Here, n (number analyzed) signifies subjects analyzed for this endpoint at specified timepoints.

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

End point timeframe:

Baseline, Week 24 and 48

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) | | |
|----------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 113 | 99 | | |
| Units: mcg/L | | | | |
| arithmetic mean (standard error) | | | | |
| Week 24: n= 103, 83 | 0.047 (± 0.0165) | 0.283 (± 0.0251) | | |
| Week 48: n= 97, 81 | 0.046 (± 0.0174) | 0.226 (± 0.0234) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Levels of Parathyroid Hormone (PTH) at Week 24 and 48

| | |
|-----------------|---|
| End point title | Change From Baseline in Levels of Parathyroid Hormone (PTH) at Week 24 and 48 |
|-----------------|---|

End point description:

Change from baseline in PTH at Week 24 and 48 were reported. BIS analysis set included all subjects who were randomized, received at least 1 dose of study drug in study and had at least one post-baseline value for either biomarker/BMD data. Here, n (number analyzed) signifies subjects analyzed for this endpoint at specified timepoints.

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

End point timeframe:

Baseline, Week 24 and 48

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) | | |
|-----------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 113 | 99 | | |
| Units: Picomol per liter (pmol/L) | | | | |
| arithmetic mean (standard error) | | | | |
| Week 24: n= 101, 83 | 0.113 (± 0.2171) | 0.777 (± 0.2401) | | |
| Week 48: n= 95, 83 | -0.004 (± 0.2232) | 0.633 (± 0.2155) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Levels of 25-Hydroxyvitamin D (25-OH Vitamin D), at Week 24 and 48

| | |
|-----------------|--|
| End point title | Change From Baseline in Levels of 25-Hydroxyvitamin D (25-OH Vitamin D), at Week 24 and 48 |
|-----------------|--|

End point description:

Change from baseline in 25-OH Vitamin D at Week 24 and 48 was reported. BIS analysis set included all subjects who were randomized, received at least 1 dose of study drug in study and had at least one post-baseline value for either biomarker/BMD data. Here, n (number analyzed) signifies subjects

analyzed for this endpoint at specified timepoints.

| | |
|---------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Weeks 24 and 48 | |

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) | | |
|-----------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 113 | 99 | | |
| Units: nanomol per liter (nmol/L) | | | | |
| arithmetic mean (standard error) | | | | |
| Week 24 n= 101, 84 | 12.7 (± 2.76) | 22.1 (± 3.76) | | |
| Week 48 n= 97, 82 | 16.9 (± 2.84) | 28.3 (± 3.15) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With HIV-1 RNA <50 Copies per mL at Week 96 Defined by FDA Snapshot Approach

| | |
|-----------------|--|
| End point title | Percentage of Subjects With HIV-1 RNA <50 Copies per mL at Week 96 Defined by FDA Snapshot Approach ^[2] |
|-----------------|--|

End point description:

Percentage of subjects with a HIV-1 RNA <50 copies per mL were assessed using FDA snapshot approach which defines a subject'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 snapshot approach classified subjects into 3 outcome categories: 1) virologic success (HIV RNA <20/50/200 copies per mL at Week 96), 2) virologic failure (HIV RNA greater than or equal to [\geq] 20/50/200 copies per mL at Week 96), 3) no viral load data in the Week 96 visit window (discontinued due to adverse event/death/other reason). The missing HIV-1 RNA is considered as non-response. The intent-to-treat (ITT) analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint.

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

Notes:

[2] - 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: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | | |
|----------------------------------|---|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 362 | 291 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 85.1 (81.0 to 88.6) | 94.2 (90.8 to 96.6) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in log10 HIV-1 RNA Levels

| | |
|-----------------|--|
| End point title | Change From Reference in log10 HIV-1 RNA Levels ^[3] |
|-----------------|--|

End point description:

Change from reference in log10 HIV-1 RNA levels were reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Based on not completed (NC) equal to (=) failure (F) analysis with values after discontinuation imputed with the baseline value. Other (intermittent) missing values are imputed using last observation carried forward (LOCF). Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint.

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

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[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: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | | |
|--------------------------------------|---|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 362 | 289 | | |
| Units: log10 HIV-1 RNA copies per mL | | | | |
| least squares mean (standard error) | -2.72 (± 0.0614) | -0.0027 (± 0.0131) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in CD4+ Cell Count

| | |
|-----------------|---|
| End point title | Change From Reference in CD4+ Cell Count ^[4] |
|-----------------|---|

End point description:

The immunologic change was determined by changes in Cluster of CD4+ cell count. Change from reference in CD4+ cell count at Week 96 were assessed. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Based on NC=F analysis with values after discontinuation imputed with the baseline value. Other (intermittent) missing values are imputed using LOCF. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint.

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

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[4] - 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: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | | |
|-------------------------------------|---|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 362 | 289 | | |
| Units: cells/mm ³ | | | | |
| least squares mean (standard error) | 228.85 (± 11.951) | 27.01 (± 9.522) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with >95% Treatment Adherence Assessed by Drug Accountability

| | |
|-----------------|--|
| End point title | Percentage of Subjects with >95% Treatment Adherence Assessed by Drug Accountability |
|-----------------|--|

End point description:

Treatment adherence assessed by drug accountability (based on pill count) from start of treatment/switch to last study drug intake by determination of the cumulative treatment adherence in subjects who returned all dispensed bottles prior to or at the last visit in the study. Adherent subjects were defined as having an adherence >95% as assessed by drug accountability. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study and n (number analyzed) signifies subjects analyzed for this outcome measure at specified timepoints. Here, 99999 refers that the data is not available for referred arm.

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

End point timeframe:

Baseline to Switch and switch to EOE to open-label D/C/F/TAF (Up to 3 years)

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) | |
|---|---|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 362 | 295 | 363 | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Baseline to Switch (double-blind) (n=289, 282, 0) | 87.2 | 0 | 82.6 | |
| Switch to EOE (open-label D/C/F/TAF) (n=231,0,222) | 92.2 | 88.7 | 99999 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Grade 3 and 4 AEs, SAEs, and Premature Discontinuations due to Adverse Events Through Week 96

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Grade 3 and 4 AEs, SAEs, and Premature Discontinuations due to Adverse Events Through Week 96 ^[5] |
|-----------------|--|

End point description:

AE is any untoward medical occurrence in subject who received study drug without regard to possibility of causal relationship. Events with Grade 3 or higher (3=Severe; 4=life-threatening; 5=fatal) are events that significantly interrupt usual daily activity. SAE is any adverse event (AE) that results in: death, persistent or significant disability/incapacity, requires inpatient hospitalization or prolongation of existing hospitalization, is life-threatening experience, is a congenital anomaly/birth defect and may jeopardize subject and/or may require medical or surgical intervention to prevent one of the outcomes listed above. The ITT analysis set included all the Subjects who were randomized and received at least one dose of study treatment in the study. This endpoint was planned to be reported for participants who received D/C/F/TAF in group 1 and who switched to D/C/F/TAF in group 2.

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

End point timeframe:

Up to Week 96

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: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | | |
|---------------------------------------|---|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 362 | 295 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Grade 3 AEs | 11.6 | 3.7 | | |
| Grade 4 AEs | 0.8 | 1.4 | | |
| SAEs | 10.8 | 2.7 | | |
| Premature discontinuations due to AEs | 2.8 | 0.3 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in Serum Creatinine

| | |
|-----------------|--|
| End point title | Change From Reference in Serum Creatinine ^[6] |
|-----------------|--|

End point description:

Change from reference in serum creatinine was reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

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

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

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: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | | |
|-------------------------------|--|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 317 | 287 | | |
| Units: mg/dL | | | | |
| median (full range (min-max)) | 0.045 (-0.25 to 0.30) | -0.034 (-0.71 to 0.40) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in eGFRcr by CKD-EPI Formula

| | |
|-----------------|---|
| End point title | Change From Reference in eGFRcr by CKD-EPI Formula ^[7] |
|-----------------|---|

End point description:

Change from reference in eGFRcr was calculated using the CKD-EPI equation as per Stage 1 (normal or high GFR) to Stage 5 (End Stage of CKD). The ITT analysis set included all the Subjects who were randomized and received at least one dose of study treatment in the study. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

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

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

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: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | | |
|-----------------------------------|---|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 317 | 287 | | |
| Units: mL/min/1.73 m ² | | | | |
| median (full range (min-max)) | -5.6 (-33 to 29) | 2.3 (-29 to 43) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in Estimated Glomerular Filtration Rate Based on Serum Creatinine by Cockcroft-Gault Formula

| | |
|-----------------|---|
| End point title | Change From Reference in Estimated Glomerular Filtration Rate Based on Serum Creatinine by Cockcroft-Gault Formula ^[8] |
|-----------------|---|

End point description:

Change from reference in eGFR_{cr} by (cockcroft-gault formula) was reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

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

End point timeframe:

This endpoint was planned to be reported for participants who received D/C/F/TAF in group 1 and who switched to D/C/F/TAF in group 2.

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: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | | |
|-------------------------------|---|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 317 | 287 | | |
| Units: mL/min | | | | |
| median (full range (min-max)) | -5.2 (-73 to 41) | 4.6 (-47 to 55) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in Estimated Glomerular Filtration Rate Based on Serum Cystatin C (eGFRcyst) by CKD-EPI Formula

| | |
|-----------------|--|
| End point title | Change From Reference in Estimated Glomerular Filtration Rate Based on Serum Cystatin C (eGFRcyst) by CKD-EPI Formula ^[9] |
|-----------------|--|

End point description:

Change from reference in eGFRcyst was calculated using the CKD-EPI equation as per Stage 1 (normal or high GFR) to Stage 5 (End Stage of CKD): <15 mL/min indicate very severe or end stage kidney failure. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

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

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

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: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | | |
|-----------------------------------|---|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 | 33 | | |
| Units: mL/min/1.73 m ² | | | | |
| median (full range (min-max)) | 4.4 (-14 to 37) | 0 (-12 to 26) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in UPCR

| | |
|-----------------|---|
| End point title | Change From Reference in UPCR ^[10] |
|-----------------|---|

End point description:

Change from reference in UPCR was reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint. This endpoint was planned to be reported for participants who received D/C/F/TAF in

Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

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

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

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: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | | |
|-------------------------------|---|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 312 | 287 | | |
| Units: mg/g | | | | |
| median (full range (min-max)) | -15.46 (-728.7 to 197.9) | -1.40 (-705.7 to 289.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in UACR

| | |
|-----------------|---|
| End point title | Change From Reference in UACR ^[11] |
|-----------------|---|

End point description:

Change from reference in UACR were reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

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

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | | |
|-------------------------------|---|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 317 | 287 | | |
| Units: mg/g | | | | |
| median (full range (min-max)) | -0.70 (-288.1 to 44.5) | -0.49 (-294.5 to 583.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in URBPCR

| | |
|-----------------|---|
| End point title | Change From Reference in URBPCR ^[12] |
|-----------------|---|

End point description:

Change from references in URBPCR was reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

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

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | | |
|-------------------------------|---|------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 313 | 285 | | |
| Units: mcg/g | | | | |
| median (full range (min-max)) | 13.70 (-1555.1 to 2547.1) | -35.53 (- 108886.3 to 291.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in UB2MGCR

| | |
|-----------------|--|
| End point title | Change From Reference in UB2MGCR ^[13] |
|-----------------|--|

End point description:

Change from reference in UB2MGCR was reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

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

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | | |
|-------------------------------|--|-----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 310 | 286 | | |
| Units: mcg/g | | | | |
| median (full range (min-max)) | -27.04 (-11704.6 to 894.7) | -40.53 (-111778.9 to 624.6) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Reference in Hip and Spine BMD

| | |
|-----------------|--|
| End point title | Percent Change From Reference in Hip and Spine BMD ^[14] |
|-----------------|--|

End point description:

The BMD is the amount of mineral in gram per square centimeter of bone, which was assessed by DEXA scan. Positive values are "best v" and negative values are "worst values" of change. Percent change from references in hip and spine BMD was assessed. BIS analysis set included all subjects who were randomized, received at least 1 dose of study drug in study and had at least one post-baseline value for either biomarker/BMD data. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and n (number analyzed) signifies subjects analyzed for this endpoint at specified timepoints. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

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

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | | |
|------------------------------|--|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 113 | 83 | | |
| Units: Percent change in BMD | | | | |

| | | | | |
|----------------------------------|---------------------|--------------------|--|--|
| arithmetic mean (standard error) | | | | |
| Hip region BMD n= 87, 71 | -0.2565 (± 0.35599) | 0.5467 (± 0.38512) | | |
| Spine region BMD n= 86, 71 | -0.9349 (± 0.44599) | 0.4829 (± 0.39270) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Reference in Urine FEPO4

| | |
|-----------------|--|
| End point title | Percent Change From Reference in Urine FEPO4 ^[15] |
|-----------------|--|

End point description:

Percent change from references in FEPO4 were reported. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

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

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[15] - 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: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | | |
|--------------------------------------|--|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 316 | 286 | | |
| Units: Percent change in urine FEPO4 | | | | |
| median (full range (min-max)) | 18.52 (-84.2 to 1170.1) | -7.51 (-83.5 to 494.7) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in BMD T-score of Hip and Spine at Week 96

| | |
|-----------------|--|
| End point title | Change From Reference in BMD T-score of Hip and Spine at Week 96 ^[16] |
|-----------------|--|

End point description:

BMD status was assessed using BMD T-scores; normal bone status was defined by a BMD T-score ≥ -1 , osteopenia by a T-score ≥ -2.5 to < -1.0 , and osteoporosis by a T-score < -2.5 . BIS analysis set included all subjects who were randomized, received at least 1 dose of study drug in study and had at least one post-baseline value for either biomarker/BMD data. Here, reference 1 is the comparative

phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint and n (number analyzed) signifies subjects analyzed for this endpoint at specified timepoints. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

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

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[16] - 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: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | | |
|-------------------------------------|--|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 87 | 71 | | |
| Units: BMD T-score | | | | |
| arithmetic mean (standard error) | | | | |
| Hip region BMD T-score (n=87, 71) | -0.016 (\pm 0.0245) | 0.025 (\pm 0.0272) | | |
| Spine region BMD T-score (n=86, 71) | -0.090 (\pm 0.0407) | 0.034 (\pm 0.0355) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in ALP Levels

| | |
|-----------------|---|
| End point title | Change From Reference in ALP Levels ^[17] |
|-----------------|---|

End point description:

Change from references in ALP levels was reported. BIS analysis set included all subjects who were randomized, received at least 1 dose of study drug in study and had at least one post-baseline value for either biomarker/BMD data. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

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

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[17] - 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: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | | |
|----------------------------------|---|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 92 | 80 | | |
| Units: U/L | | | | |
| arithmetic mean (standard error) | -0.9 (\pm 1.23) | -9.7 (\pm 1.55) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in Levels of Serum P1NP

| | |
|-----------------|---|
| End point title | Change From Reference in Levels of Serum P1NP ^[18] |
|-----------------|---|

End point description:

Change from reference in serum P1NP levels were reported. BIS analysis set included all subjects who were randomized, received at least 1 dose of study drug in study and had at least one post-baseline value for either biomarker/BMD data. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

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

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[18] - 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: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | | |
|----------------------------------|---|-------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 91 | 75 | | |
| Units: mcg/L | | | | |
| arithmetic mean (standard error) | 2.817 (\pm 1.7140) | -11.963 (\pm 1.7636) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in Levels of Serum CTX

| | |
|-----------------|--|
| End point title | Change From Reference in Levels of Serum CTX ^[19] |
|-----------------|--|

End point description:

Change from reference in serum CTX levels was reported. BIS analysis set included all subjects who were randomized, received at least 1 dose of study drug in study and had at least one post-baseline value for either biomarker/BMD data. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

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

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[19] - 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: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | | |
|----------------------------------|--|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 91 | 77 | | |
| Units: mcg/L | | | | |
| arithmetic mean (standard error) | 0.041 (\pm 0.0190) | -0.162 (\pm 0.0190) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in Levels of PTH

| | |
|-----------------|--|
| End point title | Change From Reference in Levels of PTH ^[20] |
|-----------------|--|

End point description:

Change from reference in PTH levels was reported. BIS analysis set included all subjects who were randomized, received at least 1 dose of study drug in study and had at least one post-baseline value for either biomarker/BMD data. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

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

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[20] - 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: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | | |
|----------------------------------|---|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 90 | 77 | | |
| Units: pmol/L | | | | |
| arithmetic mean (standard error) | -0.290 (\pm 0.2078) | -1.283 (\pm 0.2483) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Reference in Levels of 25-OH Vitamin D

| | |
|-----------------|--|
| End point title | Change From Reference in Levels of 25-OH Vitamin D ^[21] |
|-----------------|--|

End point description:

Change from reference in 25-OH Vitamin D levels were reported. BIS analysis set included all subjects who were randomized, received at least 1 dose of study drug in study and had at least one post-baseline value for either biomarker/BMD data. Here, reference 1 is the comparative phase baseline value in Week 48 analysis for test group and reference 2 is the last value prior to the switch for Control group and N (number of subjects analyzed) signifies subjects evaluated for this endpoint. This endpoint was planned to be reported for participants who received D/C/F/TAF in Test group and who switched to D/C/F/TAF in Switch to D/C/F/TAF group.

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

End point timeframe:

From Reference 1 to Week 96 for D/C/F/TAF Group and Reference 2 to Week 96 for Switch to D/C/F/TAF

Notes:

[21] - 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: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | | |
|----------------------------------|---|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 91 | 77 | | |
| Units: nmol/L | | | | |
| arithmetic mean (standard error) | 21.3 (\pm 2.45) | -10.3 (\pm 2.87) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With HIV RNA <50, <20, and <200 Copies/mL Post-week 96 to end of Extension

| | |
|---|---|
| End point title | Percentage of Subjects With HIV RNA <50, <20, and <200 Copies/mL Post-week 96 to end of Extension ^[22] |
| End point description: | |
| Percentage of subjects with HIV RNA <50, <20, and <200 copies/mL post week 96 to end of extension were reported. The ITT analysis set included all the Subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint and n (number analyzed) signifies subjects analyzed for this endpoint at specified timepoints. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 96 to end of extension (up to 3 years) | |

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | | |
|--|--|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 303 | 296 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Week 96 + 6 months (<50 copies/mL) n= 303, 296 | 97.7 (95.3 to 99.1) | 96.3 (93.4 to 98.1) | | |
| Week 96 + 12 months (<50 copies/mL) n= 194, 214 | 99.0 (96.3 to 99.9) | 96.7 (93.4 to 98.7) | | |
| Week 96 + 18 months (<50 copies/mL) n= 158, 167 | 98.1 (94.6 to 99.6) | 98.2 (94.8 to 99.6) | | |
| Week 96 + 24 months (<50 copies/mL) n= 81, 92 | 97.5 (91.4 to 99.7) | 95.7 (89.2 to 98.8) | | |
| Week 96 + 30 months (<50 copies/mL) n= 57, 58 | 94.7 (85.4 to 98.9) | 91.4 (81.0 to 97.1) | | |
| Week 96 + 36 months (<50 copies/mL) n= 19, 16 | 100.0 (82.4 to 100.0) | 68.8 (41.3 to 89.0) | | |
| Week 96 + 6 months (<20 copies/mL) n= 303, 296 | 85.8 (81.4 to 89.5) | 88.2 (83.9 to 91.6) | | |
| Week 96 + 12 months (<20 copies/mL) n= 194, 214 | 89.7 (84.5 to 93.6) | 91.6 (87.0 to 94.9) | | |
| Week 96 + 18 months (<20 copies/mL) n= 158, 167 | 92.4 (87.1 to 96.0) | 92.8 (87.8 to 96.2) | | |
| Week 96 + 24 months (<20 copies/mL) n= 81, 92 | 90.1 (81.5 to 95.6) | 87.0 (78.3 to 93.1) | | |
| Week 96 + 30 months (<20 copies/mL) n= 57, 58 | 89.5 (78.5 to 96.0) | 84.5 (72.6 to 92.7) | | |
| Week 96 + 36 months (<20 copies/mL) n= 19, 16 | 94.7 (74.0 to 99.9) | 62.5 (35.4 to 84.8) | | |
| Week 96 + 6 months (<200 copies/mL) n= 303, 296 | 99.7 (98.2 to 100.0) | 99.3 (97.6 to 99.9) | | |
| Week 96 + 12 months (<200 copies/mL) n= 194, 214 | 100.0 (98.1 to 100.0) | 99.5 (97.4 to 100) | | |
| Week 96 + 18 months (<200 copies/mL) n= 158, 167 | 98.7 (95.5 to 99.8) | 98.2 (94.8 to 99.6) | | |
| Week 96 + 24 months (<200 copies/mL) n= 81, 92 | 97.5 (91.4 to 99.7) | 97.8 (92.4 to 99.7) | | |
| Week 96 + 30 months (<200 copies/mL) n= 57, 58 | 96.5 (87.9 to 99.6) | 98.3 (90.8 to 100.0) | | |

| | | | | |
|--|-----------------------|---------------------|--|--|
| Week 96 + 36 months (<200 copies/mL) n= 19, 16 | 100.0 (82.4 to 100.0) | 87.5 (61.7 to 98.4) | | |
|--|-----------------------|---------------------|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Protocol-defined Virologic Failure (PDVF)

| | |
|--|---|
| End point title | Percentage of Subjects with Protocol-defined Virologic Failure (PDVF) |
| End point description: | |
| Percentage of subjects with PDVF were reported. PDVF was defined as having virologic non-response (HIV-1 RNA <1 log10 reduction from baseline and ≥50 copies/mL at the Week 8 visit, confirmed at the next visit), virologic rebound (confirmed HIV-1 RNA ≥50 copies/mL after confirmed consecutive HIV-1 RNA <50 copies/mL or confirmed >1 log10 increase in HIV-1 RNA from nadir), or viremic at final time point (final available on treatment HIV-1 RNA ≥400 copies/mL). The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here N (number of participants analyzed) refers to 311 for test group and 310 for switch to D/C/F/TAF group. Here,99999 refers that the data is not applicable for the respective arm as specified below because data of Baseline to Week 96 is applicable for Test group, Baseline to switch applicable for Control group and Switch to Week 96 is applicable to switch to D/C/F/TAF group. | |
| End point type | Secondary |
| End point timeframe: | |
| From Baseline up to Week 96 | |

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) | |
|---|---|---------------------|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 362 | 295 | 363 | |
| Units: percentage of subject | | | | |
| number (not applicable) | | | | |
| Subjects who met PDVF (Baseline - Week 96) | 4.1 | 99999 | 99999 | |
| Virologic non-response (Baseline - Week 96) | 0.6 | 99999 | 99999 | |
| Virologic rebound (Baseline-Week 96) | 0.3 | 99999 | 99999 | |
| Viremic at final time point (Baseline-Week 96) | 0.6 | 99999 | 99999 | |
| Subjects who met PDVF (Baseline - Switch) | 99999 | 99999 | 4.4 | |
| Virologic non-response (Baseline - Switch) | 99999 | 99999 | 0 | |
| Virologic rebound (Baseline - Switch) | 99999 | 99999 | 3.9 | |
| Viremic at final time point (Baseline - Switch) | 99999 | 99999 | 0.6 | |
| Subjects who met PDVF (Switch - Week 96) | 99999 | 1.1 | 99999 | |

| | | | | |
|--|-------|-----|-------|--|
| Virologic non-response (Switch - Week 96) | 99999 | 0 | 99999 | |
| Virologic rebound (Switch - Week 96) | 99999 | 1.1 | 99999 | |
| Viremic at final time point (Switch - Week 96) | 99999 | 0 | 99999 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with PDVF Post-week 96 to End of Extension

| | |
|-----------------|---|
| End point title | Percentage of Subjects with PDVF Post-week 96 to End of Extension ^[23] |
|-----------------|---|

End point description:

Percentage of subjects with PDVF were reported. PDVF was defined as having virologic non-response (HIV-1 RNA <1 log₁₀ reduction from baseline and ≥50 copies/mL at the Week 8 visit, confirmed at the next visit), virologic rebound (confirmed HIV-1 RNA ≥50 copies/mL after confirmed consecutive HIV-1 RNA <50 copies/mL or confirmed >1 log₁₀ increase in HIV-1 RNA from nadir), or viremic at final time point (final available on treatment HIV-1 RNA ≥400 copies/mL). The ITT analysis set included all the Subjects who were randomized and received at least one dose of study treatment in the study.

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

End point timeframe:

Week 96 to end of extension (up to 3 years)

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | | |
|------------------------------|--|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 311 | 310 | | |
| Units: percentage of subject | | | | |
| number (not applicable) | | | | |
| Subjects who met PDVF | 1.0 | 2.1 | | |
| Virologic non-response | 0 | 0 | | |
| Virologic rebound | 1.0 | 1.4 | | |
| Viremic at final time point | 0 | 0.7 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with non-PDVF by Kaplan-Meier Estimates

| | |
|-----------------|--|
| End point title | Percentage of Participants with non-PDVF by Kaplan-Meier Estimates ^[24] |
|-----------------|--|

End point description:

Percentage of participants with non-PDVF by Kaplan-Meier Estimates were reported. PDVF was defined as having virologic non-response (HIV-1 RNA <1 log10 reduction from baseline and ≥50 copies/mL at the Week 8 visit, confirmed at the next visit), virologic rebound (confirmed HIV-1 RNA ≥50 copies/mL after confirmed consecutive HIV-1 RNA <50 copies/mL or confirmed >1 log10 increase in HIV-1 RNA from nadir), or viremic at final time point (final available on treatment HIV-1 RNA ≥400 copies/mL). The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study.

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

End point timeframe:

From Week 96 to end of extension (up to 2 years and 6 months)

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | | |
|----------------------------------|--|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 311 | 310 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Week 96 | 100 (100 to 100) | 100 (100 to 100) | | |
| Week 96 + 6 months | 99.6 (97.2 to 99.9) | 99.2 (97.0 to 99.8) | | |
| Week 96 + 12 months | 99.6 (97.2 to 99.9) | 99.2 (97.2 to 99.8) | | |
| Week 96 + 18 months | 98.6 (94.0 to 99.7) | 97.8 (94.1 to 99.2) | | |
| Week 96 + 24 months | 97.3 (91.0 to 99.2) | 97.8 (94.1 to 99.2) | | |
| Week 96 + 30 months | 97.3 (91.0 to 99.2) | 92.5 (79.8 to 97.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with time to Treatment Failure by Kaplan-Meier Estimates

| | |
|-----------------|---|
| End point title | Percentage of Participants with time to Treatment Failure by Kaplan-Meier Estimates ^[25] |
|-----------------|---|

End point description:

Percentage of participants with time to treatment failure by Kaplan-Meier Estimates were reported. Treatment failure was defined as having either protocol-defined virologic failure or having discontinued for reasons other than alternate access to D/C/F/TAF (or other ARVs). The ITT analysis set included all the Subjects who were randomized and received at least one dose of study treatment in the study. Here, 99999 stands for data not available for the referred arm as the participants didn't have treatment failure at this timepoint.

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

End point timeframe:

From Week 96 to end of extension (up to 3 years)

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | | |
|----------------------------------|---|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 311 | 310 | | |
| Units: months | | | | |
| number (confidence interval 95%) | | | | |
| Week 96 | 100 (100 to 100) | 100 (100 to 100) | | |
| Week 96 + 6 months | 98.9 (96.5 to 99.6) | 97.4 (94.5 to 98.7) | | |
| Week 96 + 12 months | 95.6 (91.7 to 97.7) | 94.1 (90.2 to 96.5) | | |
| Week 96 + 18 months | 90.6 (84.9 to 94.2) | 89.5 (84.3 to 93.0) | | |
| Week 96 + 24 months | 87.1 (79.8 to 91.8) | 86.4 (80.0 to 90.9) | | |
| Week 96 + 30 months | 84.8 (75.8 to 90.6) | 79.1 (68.9 to 86.3) | | |
| Week 96 + 36 months | 84.8 (75.8 to 90.6) | 99999 (99999 to 99999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: CD4+ Cell Count Post-Week 96 to end of Extension

| | |
|-----------------|--|
| End point title | CD4+ Cell Count Post-Week 96 to end of Extension ^[26] |
|-----------------|--|

End point description:

The immunologic change was determined by CD4+ cell count. CD4+ cell count post-Week 96 to end of extension were assessed. The ITT analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint and n (number analyzed) signifies subjects analyzed for this endpoint at specified timepoints.

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

End point timeframe:

Week 96 to end of extension (up to 3 years)

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | | |
|-------------------------------------|---|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 300 | 293 | | |
| Units: cells/mm ³ | | | | |
| least squares mean (standard error) | | | | |
| Week 96 + 6 months n= 300, 293 | 790.2 (± 17.23) | 749.7 (± 16.44) | | |
| Week 96 + 12 months n= 192, 212 | 779.4 (± 22.45) | 774.3 (± 21.91) | | |
| Week 96 + 18 months n= 154, 165 | 789.8 (± 23.43) | 758.4 (± 23.25) | | |
| Week 96 + 24 months n= 78, 92 | 781.9 (± 37.77) | 784.1 (± 30.78) | | |
| Week 96 + 30 months n= 57, 58 | 741.6 (± 37.12) | 736.7 (± 37.47) | | |
| Week 96 + 36 months n= 18, 16 | 784.7 (± 69.74) | 778.4 (± 86.59) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With ARV Resistance

| | |
|--|--|
| End point title | Number of Subjects With ARV Resistance |
| End point description: | |
| Number of subjects with DRV, FTC, TDF/TAF resistance were reported. The ITT analysis set included all the Subjects who were randomized and received at least one dose of study treatment in the study. Here, N (number of subjects analyzed) signifies subjects evaluated for this endpoint. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to end of extension (up to 4 years) | |

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) | |
|---|---|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 12 | 7 | 8 | |
| Units: subjects | | | | |
| DRV resistance-associated mutations (RAMs) | 0 | 0 | 0 | |
| TFV RAMs | 0 | 0 | 0 | |
| FTC RAMs | 2 | 2 | 1 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Grade 3 and 4 AEs, SAEs, and Premature Discontinuations due to Adverse Events Post-Week 96 to end of Extension

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Grade 3 and 4 AEs, SAEs, and Premature Discontinuations due to Adverse Events Post-Week 96 to end of Extension ^[27] |
|-----------------|--|

End point description:

AE is any untoward medical occurrence in subject who received study drug without regard to possibility of causal relationship. Events with Grade 3 or higher (3=Severe; 4=life-threatening; 5=fatal) are events that significantly interrupt usual daily activity, require systemic drug therapy/other treatment and are, in many situations, considered unacceptable or intolerable events. SAE is any adverse event (AE) that results in: death, persistent or significant disability/incapacity, requires inpatient hospitalization or prolongation of existing hospitalization, is life-threatening experience, is a congenital anomaly/birth defect and may jeopardize subject and/or may require medical or surgical intervention to prevent one of the outcomes listed above. The ITT analysis set included all the Subjects who were randomized and received at least one dose of study treatment in the study.

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

End point timeframe:

From Week 96 to end of extension (up to 3 years)

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As planned the endpoint is not reporting Stats for all the arms of the baseline period.

| End point values | D/C/F/TAF (Test) (Baseline [BL] to End of Extension [EOE]) | Switch to D/C/F/TAF | | |
|---------------------------------------|---|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 311 | 310 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Grade 3 AEs | 3.5 | 5.2 | | |
| Grade 4 AEs | 0 | 1.3 | | |
| SAEs | 3.2 | 4.8 | | |
| Premature discontinuations due to AEs | 1.0 | 1.3 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 60 months

Adverse event reporting additional description:

The intent-to-treat (ITT) analysis set included all the subjects who were randomized and received at least one dose of study treatment in the study.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

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

| | |
|--------------------|----|
| Dictionary version | 23 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|---|
| Reporting group title | D/C/F/TAF (Test) (Baseline to End of Extension [EOE]) |
|-----------------------|---|

Reporting group description:

Subjects received a single oral tablet containing darunavir (DRV) 800 milligram (mg)/ cobicistat (COBI) 150 mg/ emtricitabine (FTC) 200 mg/ tenofovir alafenamide (TAF) 10 mg (D/C/F/TAF fixed dose combination [FDC]) once daily along with DRV/COBI FDC-matching placebo and FTC/tenofovir disoproxil fumarate (TDF) FDC-matching placebo tablets once daily up to Week 48 analysis unblinding visit (that is, after last subject has reached Week 48). After Week 48 analysis unblinding visit, all subjects received D/C/F/TAF treatment up to Week 96. After Week 96, subjects were given the opportunity to continue D/C/F/TAF treatment during an extension phase until the D/C/F/TAF FDC tablet became commercially available.

| | |
|-----------------------|--|
| Reporting group title | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) |
|-----------------------|--|

Reporting group description:

Subjects received DRV 800 mg/COBI 150 mg FDC and FTC 200 mg/TDF 300 mg FDC along with D/C/F/TAF FDC-matching placebo tablet once daily. Subjects received DRV 800 mg/COBI 150 mg FDC and FTC 200 mg/TDF 300 mg FDC along with D/C/F/TAF FDC-matching placebo tablet once daily up to Week 48 analysis unblinding visit (that is, after last subject has reached Week 48).

| | |
|-----------------------|---------------------------|
| Reporting group title | Switch to D/C/F/TAF Group |
|-----------------------|---------------------------|

Reporting group description:

After Week 48 analysis unblinding visit, subjects earlier receiving treatment with DRV/COBI+ FTC/TDF (Control) switched to D/C/F/TAF treatment and continued for up to Week 96 during open-label, single-group treatment phase. After Week 96, subjects were given the opportunity to continue D/C/F/TAF treatment until the D/C/F/TAF FDC tablet became commercially available.

| Serious adverse events | D/C/F/TAF (Test) (Baseline to End of Extension [EOE]) | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) | Switch to D/C/F/TAF Group |
|---|---|--|------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 47 / 362 (12.98%) | 36 / 363 (9.92%) | 21 / 322 (6.52%) |
| number of deaths (all causes) | 0 | 1 | 1 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Anogenital Warts | | | |
| subjects affected / exposed | 2 / 362 (0.55%) | 2 / 363 (0.55%) | 0 / 322 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|-----------------|-----------------|-----------------|
| Basal Cell Carcinoma | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Hodgkin's Disease | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 1 / 363 (0.28%) | 0 / 322 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Kaposi's Sarcoma | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 1 / 363 (0.28%) | 0 / 322 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Squamous Cell Carcinoma of Lung | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 1 / 363 (0.28%) | 0 / 322 (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 |
| Vascular disorders | | | |
| Thrombosis | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| General disorders and administration site conditions | | | |
| Influenza Like Illness | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 1 / 363 (0.28%) | 0 / 322 (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 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 1 / 363 (0.28%) | 1 / 322 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-Cardiac Chest Pain | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 1 / 363 (0.28%) | 1 / 322 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Vascular Stent Stenosis | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 1 / 363 (0.28%) | 0 / 322 (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 |
| Social circumstances | | | |
| Alcohol Use | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 0 / 363 (0.00%) | 1 / 322 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Ovarian Cyst Ruptured | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Testicular Torsion | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 0 / 363 (0.00%) | 1 / 322 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uterine Polyp | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthmatic Crisis | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Haemoptysis | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Pneumothorax | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 1 / 322 (0.31%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Borderline Personality Disorder | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 0 / 363 (0.00%) | 1 / 322 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Depression | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Drug Dependence | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Suicide Attempt | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 3 / 363 (0.83%) | 1 / 322 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicidal Ideation | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 1 / 363 (0.28%) | 2 / 322 (0.62%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Waist Circumference Increased | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 | | | |
| Concussion | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Alcohol Poisoning | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 1 / 363 (0.28%) | 0 / 322 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Exposure During Pregnancy | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Foot Fracture | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Humerus Fracture | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 1 / 363 (0.28%) | 0 / 322 (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 |
| Intentional Overdose | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 0 / 363 (0.00%) | 1 / 322 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Limb Injury | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 0 / 363 (0.00%) | 1 / 322 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lumbar Vertebral Fracture | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Overdose | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 0 / 363 (0.00%) | 1 / 322 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Road Traffic Accident | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 362 (0.00%) | 1 / 363 (0.28%) | 0 / 322 (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 |
| Tendon Rupture | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 1 / 363 (0.28%) | 0 / 322 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper Limb Fracture | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Cardiac disorders | | | |
| Myocardial Infarction | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 0 / 363 (0.00%) | 1 / 322 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Cerebrovascular Accident | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 0 / 363 (0.00%) | 1 / 322 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dizziness Postural | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 1 / 363 (0.28%) | 0 / 322 (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 |
| Headache | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 0 / 363 (0.00%) | 1 / 322 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Polyneuropathy | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 0 / 363 (0.00%) | 1 / 322 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 362 (0.00%) | 0 / 363 (0.00%) | 1 / 322 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient Ischaemic Attack | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Blood and lymphatic system disorders | | | |
| Bone Marrow Oedema | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 1 / 363 (0.28%) | 0 / 322 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaemia | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 | | | |
| Anal Fistula | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 1 / 363 (0.28%) | 0 / 322 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anogenital Dysplasia | | | |
| subjects affected / exposed | 2 / 362 (0.55%) | 1 / 363 (0.28%) | 0 / 322 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Hepatobiliary disorders | | | |
| Cholangitis Sclerosing | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 1 / 363 (0.28%) | 0 / 322 (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 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 2 / 363 (0.55%) | 0 / 322 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Stevens-Johnson Syndrome | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 1 / 363 (0.28%) | 0 / 322 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Toxic Skin Eruption | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 2 / 363 (0.55%) | 0 / 322 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Calculus Urinary | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Haematuria | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Hydronephrosis | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 1 / 363 (0.28%) | 0 / 322 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Back Pain | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Fistula | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Osteoarthritis | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Intervertebral Disc Protrusion | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 1 / 363 (0.28%) | 0 / 322 (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 |
| Osteoporosis | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 1 / 363 (0.28%) | 0 / 322 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Anal Abscess | | | |
| subjects affected / exposed | 2 / 362 (0.55%) | 1 / 363 (0.28%) | 0 / 322 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abscess Limb | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Appendicitis | | | |
| subjects affected / exposed | 3 / 362 (0.83%) | 2 / 363 (0.55%) | 1 / 322 (0.31%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Clostridium Difficile Colitis | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 1 / 363 (0.28%) | 0 / 322 (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 |
| Diarrhoea Infectious | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 0 / 363 (0.00%) | 1 / 322 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Erysipelas | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 0 / 363 (0.00%) | 2 / 322 (0.62%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatitis A | | | |
| subjects affected / exposed | 3 / 362 (0.83%) | 3 / 363 (0.83%) | 2 / 322 (0.62%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Hepatitis Viral | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Influenza | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Herpes Zoster | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Latent Syphilis | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 1 / 363 (0.28%) | 0 / 322 (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 |
| Myocarditis Infectious | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 1 / 363 (0.28%) | 0 / 322 (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 |
| Mumps | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 1 / 363 (0.28%) | 0 / 322 (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 Bacterial | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Lung Abscess | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Papilloma Viral Infection | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 1 / 363 (0.28%) | 0 / 322 (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 |
| Neurosyphilis | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Pneumonia | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 3 / 362 (0.83%) | 1 / 363 (0.28%) | 0 / 322 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal Abscess | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 1 / 363 (0.28%) | 0 / 322 (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 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 1 / 363 (0.28%) | 0 / 322 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Secondary Syphilis | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Urethritis | | | |
| subjects affected / exposed | 0 / 362 (0.00%) | 0 / 363 (0.00%) | 1 / 322 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syphilis | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 1 / 363 (0.28%) | 1 / 322 (0.31%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral Infection | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 |
| Urinary Tract Infection | | | |
| subjects affected / exposed | 1 / 362 (0.28%) | 0 / 363 (0.00%) | 0 / 322 (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 | D/C/F/TAF (Test) (Baseline to End of Extension [EOE]) | DRV/COBI+ FTC/TDF (Control) (Baseline to Switch) | Switch to D/C/F/TAF Group |
|--|---|--|------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 284 / 362 (78.45%) | 252 / 363 (69.42%) | 137 / 322 (42.55%) |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 56 / 362 (15.47%) | 38 / 363 (10.47%) | 11 / 322 (3.42%) |
| occurrences (all) | 79 | 66 | 12 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 26 / 362 (7.18%) | 21 / 363 (5.79%) | 1 / 322 (0.31%) |
| occurrences (all) | 29 | 24 | 1 |
| Asthenia | | | |
| subjects affected / exposed | 21 / 362 (5.80%) | 15 / 363 (4.13%) | 4 / 322 (1.24%) |
| occurrences (all) | 21 | 16 | 4 |
| Pyrexia | | | |
| subjects affected / exposed | 20 / 362 (5.52%) | 24 / 363 (6.61%) | 6 / 322 (1.86%) |
| occurrences (all) | 22 | 28 | 6 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 89 / 362 (24.59%) | 72 / 363 (19.83%) | 18 / 322 (5.59%) |
| occurrences (all) | 143 | 91 | 20 |
| Nausea | | | |
| subjects affected / exposed | 34 / 362 (9.39%) | 46 / 363 (12.67%) | 8 / 322 (2.48%) |
| occurrences (all) | 39 | 56 | 8 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 20 / 362 (5.52%) | 15 / 363 (4.13%) | 7 / 322 (2.17%) |
| occurrences (all) | 24 | 16 | 7 |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 37 / 362 (10.22%) | 25 / 363 (6.89%) | 9 / 322 (2.80%) |
| occurrences (all) | 44 | 26 | 9 |
| Psychiatric disorders | | | |

| | | | |
|--|--------------------------|-------------------------|------------------------|
| Anxiety subjects affected / exposed occurrences (all) | 19 / 362 (5.25%) 21 | 9 / 363 (2.48%) 10 | 5 / 322 (1.55%) 5 |
| Insomnia subjects affected / exposed occurrences (all) | 20 / 362 (5.52%) 24 | 13 / 363 (3.58%) 14 | 5 / 322 (1.55%) 5 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 20 / 362 (5.52%) 25 | 17 / 363 (4.68%) 20 | 11 / 322 (3.42%) 12 |
| Back Pain subjects affected / exposed occurrences (all) | 31 / 362 (8.56%) 36 | 10 / 363 (2.75%) 11 | 16 / 322 (4.97%) 18 |
| Osteopenia subjects affected / exposed occurrences (all) | 19 / 362 (5.25%) 20 | 29 / 363 (7.99%) 32 | 0 / 322 (0.00%) 0 |
| Infections and infestations | | | |
| Bronchitis subjects affected / exposed occurrences (all) | 24 / 362 (6.63%) 32 | 25 / 363 (6.89%) 30 | 20 / 322 (6.21%) 22 |
| Chlamydial Infection subjects affected / exposed occurrences (all) | 23 / 362 (6.35%) 27 | 9 / 363 (2.48%) 9 | 2 / 322 (0.62%) 2 |
| Gastroenteritis subjects affected / exposed occurrences (all) | 28 / 362 (7.73%) 32 | 15 / 363 (4.13%) 15 | 5 / 322 (1.55%) 5 |
| Gonorrhoea subjects affected / exposed occurrences (all) | 21 / 362 (5.80%) 31 | 14 / 363 (3.86%) 15 | 5 / 322 (1.55%) 6 |
| Pharyngitis subjects affected / exposed occurrences (all) | 31 / 362 (8.56%) 34 | 19 / 363 (5.23%) 24 | 7 / 322 (2.17%) 7 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 64 / 362 (17.68%) 102 | 38 / 363 (10.47%) 58 | 19 / 322 (5.90%) 23 |
| Respiratory Tract Infection | | | |

| | | | |
|------------------------------------|-------------------|------------------|------------------|
| subjects affected / exposed | 20 / 362 (5.52%) | 14 / 363 (3.86%) | 8 / 322 (2.48%) |
| occurrences (all) | 28 | 22 | 11 |
| Upper Respiratory Tract Infection | | | |
| subjects affected / exposed | 40 / 362 (11.05%) | 30 / 363 (8.26%) | 26 / 322 (8.07%) |
| occurrences (all) | 55 | 42 | 43 |
| Syphilis | | | |
| subjects affected / exposed | 41 / 362 (11.33%) | 25 / 363 (6.89%) | 24 / 322 (7.45%) |
| occurrences (all) | 51 | 29 | 27 |
| Metabolism and nutrition disorders | | | |
| Vitamin D Deficiency | | | |
| subjects affected / exposed | 28 / 362 (7.73%) | 16 / 363 (4.41%) | 6 / 322 (1.86%) |
| occurrences (all) | 32 | 16 | 6 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|--------------|--|
| 23 July 2015 | The overall reason for the amendment was that, following Health Authority feedback, the creatinine clearance threshold for eligibility was increased from 50 to 70 milliliters per minute (mL/min) and subjects previously treated with post-exposure prophylaxis and/or pre-exposure prophylaxis were no longer allowed in the study. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported