# Clinical trial results:
# A MULTICENTER, RANDOMIZED, DOUBLE-BLIND, COMPARATIVE TRIAL OF MARAVIROC + DARUNAVIR/RITONAVIR VERSUS EMTRICITABINE/TENOFOVIR + DARUNAVIR/RITONAVIR FOR THE TREATMENT OF ANTIRETROVIRAL-NAÏVE HIV-INFECTED PATIENTS WITH CCR5-TROPIC HIV-1

## Summary

| | |
|---|---|
| EudraCT number | 2010-021785-30 |
| Trial protocol | DE HU SE FI BE ES GB AT DK NL PT PL IT |
| Global end of trial date | 28 January 2014 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 19 April 2016 |
| First version publication date | 16 July 2015 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | A4001095 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01345630 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | ViiV Healthcare |
| Sponsor organisation address | 980 Great West Road, Brentford, Middlesex, United Kingdom, TW8 9GS |
| Public contact | ClinicalTrial.gov Call Center, Pfizer Inc., 1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact | ClinicalTrial.gov Call Center, Pfizer Inc., 1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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 | 28 January 2014 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 30 August 2013 |
| Global end of trial reached? | Yes |
| Global end of trial date | 28 January 2014 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

To assess whether maraviroc (SelzentryTM, Celsentri®) administered once daily (QD) is non-inferior to a reference regimen of emtricitabine/tenofovir administered QD each in combination with darunavir/ritonavir in the treatment of antiretroviral naïve HIV-1 infected subjects as measured by the proportion of subjects with HIV-1 RNA below the limits of assay detection (<50 copies of HIV-1 RNA per milliliter of plasma) at Week 48.

Protection of trial subjects:

This study was conducted in accordance by all applicable legal and regulatory requirements, as well as the general principles set forth in the International Ethical Guidelines for Biomedical Research Involving Human Subjects (Council for International Organizations of Medical Sciences 2002), Guidelines for Good Clinical Practice (GCP) (International Conference on Harmonization [ICH] 1996), and the Declaration of Helsinki (World Medical Association 2008). In addition, the study was conducted in accordance with the Clinical Study Protocol (CSP), and applicable local regulatory requirements and laws.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 29 September 2011 |
| 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 | Australia: 16 |
| Country: Number of subjects enrolled | Belgium: 28 |
| Country: Number of subjects enrolled | Canada: 48 |
| Country: Number of subjects enrolled | Denmark: 3 |
| Country: Number of subjects enrolled | Finland: 3 |
| Country: Number of subjects enrolled | France: 47 |
| Country: Number of subjects enrolled | Germany: 160 |
| Country: Number of subjects enrolled | Hungary: 21 |
| Country: Number of subjects enrolled | Italy: 18 |
| Country: Number of subjects enrolled | Netherlands: 2 |
| Country: Number of subjects enrolled | Poland: 40 |
| Country: Number of subjects enrolled | Portugal: 29 |
| Country: Number of subjects enrolled | Puerto Rico: 28 |
| Country: Number of subjects enrolled | Spain: 76 |
| Country: Number of subjects enrolled | Sweden: 15 |
| Country: Number of subjects enrolled | Switzerland: 11 |

| | |
|---|---|
| Country: Number of subjects enrolled | United Kingdom: 21 |
| Country: Number of subjects enrolled | United States: 231 |
| Worldwide total number of subjects | 797 |
| EEA total number of subjects | 463 |

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) | 789 |
| From 65 to 84 years | 8 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Overall, 1423 participants were screened and 813 participants randomized in the study. A total of 797 participants were treated (396 were treated in the maraviroc + darunavir/ritonavir [MVC+DRV/r] group and 401 in the emtricitabine/tenofovir + darunavir/ritonavir [FTC/TDF+DRV/r] group). The study was conducted in 138 sites in 18 countries.

### Pre-assignment

Screening details:

Participants were randomized to undergo either genotype testing or enhanced sensitivity trofile assay (ESTA) in a 1:1 ratio. Among participants who were identified as being infected with R5 tropic HIV-1 by either testing method, 813 were randomized in a 1:1 ratio to receive 96-week treatment either in the MVC+DRV/r arm or in the FTC/TDF+DRV/r arm.

### Period 1

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

Blinding implementation details:

Randomization to tropism testing at Screening was by telephone call or via the internet by the site staff to the Interactive Voice Response System (IVRS). The results of the tropism testing were reported to the site and the participant was identified as being infected with R5 tropic HIV-1 or not, without disclosure of the type of test (genotype or trofile) performed. MVC and FTC/TDF were administered in double-blind fashion; DRV/r was administered in an open-label fashion.

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | MVC+DRV/r |

Arm description:

Participants infected with R5 HIV-1 received oral tablets of Maraviroc 150 mg once daily plus darunavir/ritonavir 800/100 mg once daily.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Maraviroc |
| Investigational medicinal product code | UK-427,857 |
| Other name | Selzentry™, Celsentri® |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

MVC tablets were orally administered 150 mg dosage units in combination with DRV/r (800/100 mg QD).

| | |
|---|---|
| **Arm title** | FTC/TDF+DRV/r |

Arm description:

Participants infected with R5 HIV-1 received oral tablets of emtricitabine/tenofovir 200/300 mg once daily plus darunavir/ritonavir 800/100 mg once daily.

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Emtricitabine & Tenofovir |
| Investigational medicinal product code | |
| Other name | Truvada |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

FTC/TDF tablets were orally administered as 200/300 mg dosage units in combination with DRV/r (800/100 mg QD).

| **Number of subjects in period 1** | MVC+DRV/r | FTC/TDF+DRV/r |
|---|---|---|
| Started | 396 | 401 |
| Completed | 35 | 42 |
| Not completed | 361 | 359 |
| Consent withdrawn by subject | 9 | 12 |
| Study terminated by Sponsor | 254 | 285 |
| Protocol violation | 4 | 1 |
| Pregnancy | 1 | 2 |
| Adverse event | 22 | 23 |
| Other reasons | 6 | 8 |
| Medication error without associated AE | - | 1 |
| Lost to follow-up | 17 | 16 |
| Insufficient clinical response | 48 | 11 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | MVC+DRV/r |
| Reporting group description: | |
| Participants infected with R5 HIV-1 received oral tablets of Maraviroc 150 mg once daily plus darunavir/ritonavir 800/100 mg once daily. | |
| Reporting group title | FTC/TDF+DRV/r |
| Reporting group description: | |
| Participants infected with R5 HIV-1 received oral tablets of emtricitabine/tenofovir 200/300 mg once daily plus darunavir/ritonavir 800/100 mg once daily. | |

| Reporting group values | MVC+DRV/r | FTC/TDF+DRV/r | Total |
|---|---|---|---|
| Number of subjects | 396 | 401 | 797 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | | 0 |
| Preterm newborn infants (gestational age < 37 wks) | | | 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) | | | 0 |
| From 65-84 years | | | 0 |
| 85 years and over | | | 0 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 37.9 | 36.2 | |
| standard deviation | ± 10.9 | ± 10.9 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 36 | 34 | 70 |
| Male | 360 | 367 | 727 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | MVC+DRV/r |
| Reporting group description: | |
| Participants infected with R5 HIV-1 received oral tablets of Maraviroc 150 mg once daily plus darunavir/ritonavir 800/100 mg once daily. | |
| Reporting group title | FTC/TDF+DRV/r |
| Reporting group description: | |
| Participants infected with R5 HIV-1 received oral tablets of emtricitabine/tenofovir 200/300 mg once daily plus darunavir/ritonavir 800/100 mg once daily. | |
| Subject analysis set title | MVC+DRV/r - Baseline |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| Participants infected with R5 HIV-1 received oral tablets of Maraviroc 150 mg once daily plus darunavir/ritonavir 800/100 mg once daily. Summary of tropism results by Baseline. | |
| Subject analysis set title | MVC+DRV/r - Failure |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| Participants infected with R5 HIV-1 received oral tablets of Maraviroc 150 mg once daily plus darunavir/ritonavir 800/100 mg once daily. Summary of tropism results corresponding to time point at or after PDTF. | |
| Subject analysis set title | FTC/TDF+DRV/r - Baseline |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| Participants infected with R5 HIV-1 received oral tablets of emtricitabine/tenofovir 200/300 mg once daily plus darunavir/ritonavir 800/100 mg once daily. Summary of tropism results by Baseline. | |
| Subject analysis set title | FTC/TDF+DRV/r - Failure |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| Participants infected with R5 HIV-1 received oral tablets of emtricitabine/tenofovir 200/300 mg once daily plus darunavir/ritonavir 800/100 mg once daily. Summary of tropism results corresponding to time point at or after PDTF. | |

### Primary: Percentage of participants with plasma HIV-1 RNA <50 copies/mL at Week 48

| | |
|---|---|
| End point title | Percentage of participants with plasma HIV-1 RNA <50 copies/mL at Week 48 |
| End point description: | |
| The proportion of participants who achieved HIV-1 RNA <50 copies/mL at week 48 was assessed according to Food and Drug Administration's (FDA's) Missing, Switch, Discontinuation'=Failure (MSDF) Snapshot algorithm. The algorithm used the plasma HIV-1 RNA in the Week 48 visit window, followed the "virology-first principle" and considers a participant who has a missing plasma HIV-1 RNA, or switches to prohibited ARV regimen or discontinues from the study or study drug for any reason, or dies, as a failure. The Full Analysis Set (FAS) consisted of all randomized participants who received at least one dose of the study drug. The missing value was imputed per FDA's MSDF Snapshot algorithm as described under "End point Description" above. | |
| End point type | Primary |
| End point timeframe: | |
| Week 48 | |

| End point values | MVC+DRV/r | FTC/TDF+DRV/r | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 396 | 401 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 77.3 | 86.8 | | |

### Statistical analyses

| Statistical analysis title | Participants with plasma HIV-1 RNA <50 copies/mL |
|---|---|
| Comparison groups | MVC+DRV/r v FTC/TDF+DRV/r |
| Number of subjects included in analysis | 797 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[1] |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -9.54 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -14.83 |
| upper limit | -4.24 |

Notes:

[1] - For the analysis of the primary endpoint conducted at Week 48, the alternative hypothesis was to test for non-inferiority of MVC+DRV/r to FTC/TDF+DRV/r with a non-inferiority margin of -10%.The difference in the percentages between the maraviroc and the emtricitabine/tenofovir treatment arms and the 2-sided 95% confidence interval for the difference was provided using the stratum-adjusted Mantel-Haenszel (MH) method over the two assays and the screening plasma HIV-1 RNA levels.

### Secondary: Frequency of adverse events (AE)

| End point title | Frequency of adverse events (AE) |
|---|---|
| End point description: | |
| Number of participants with treatment-emergent non-serious AEs. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 96/End of Study | |

| End point values | MVC+DRV/r | FTC/TDF+DRV/r | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 396 | 401 | | |
| Units: Participants | 360 | 365 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with grade 3 or 4 AEs

| End point title | Number of participants with grade 3 or 4 AEs |
|---|---|

End point description:

Number of participants with grade 3 or 4 AEs are presented below.

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

End point timeframe:

Week 96

| End point values | MVC+DRV/r | FTC/TDF+DRV/r | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 396 | 401 | | |
| Units: participants | 65 | 71 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants who discontinued due to AEs

| End point title | Number of participants who discontinued due to AEs |
|---|---|

End point description:

Number of participants who discontinued due to AEs are reported here. Three participants (two from the MVC+DRV/r arm and one from the FTC/TDF+DRV/r arm) were not considered as discontinued due to AE because other reasons for discontinuation were categorized for these participants.

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

End point timeframe:

Week 96

| End point values | MVC+DRV/r | FTC/TDF+DRV/r | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 396 | 401 | | |
| Units: Participants | 316 | 361 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of treatment-related AEs

| End point title | Number of treatment-related AEs |
|---|---|

End point description:

Number of treatment-related AEs are presented below.

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

End point timeframe:

Week 96

| End point values | MVC+DRV/r | FTC/TDF+DRV/r | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 396 | 401 | | |
| Units: participants | | | | |
| number (not applicable) | 316 | 361 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with treatment-emergent serious adverse events

| End point title | Number of participants with treatment-emergent serious adverse events |
|---|---|

End point description:

Total number of participants with treatment-emergent serious adverse events are reported.

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

End point timeframe:

Week 96

| End point values | MVC+DRV/r | FTC/TDF+DRV/r | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 396 | 401 | | |
| Units: participants | | | | |
| number (not applicable) | 41 | 40 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with Abnormal Laboratory Values

| End point title | Number of participants with Abnormal Laboratory Values |
|---|---|

End point description:

Number of participants with laboratory abnormalities are reported. In all other situations, participants who met the below criteria were carefully evaluated: 1. Any participant (with normal Baseline) who developed a Grade 3 abnormality (with the exception of hypercholesterolemia, hypertriglyceridemia, asymptomatic CPK elevations, or asymptomatic amylase or lipase elevations). 2. Any participant with Grade 1 abnormal Baseline who developed a Grade 3 abnormality and a level 2 times that of Baseline

(with the exception of hypercholesterolemia, hypertriglyceridemia, asymptomatic CPK elevations, or asymptomatic amylase or lipase elevations). 3. All participants who developed a Grade 4 laboratory abnormality. Participants with lab abnormalities who had normal values at Baseline and participants with lab abnormalities who had abnormal values at Baseline are mentioned below in the table.

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

| **End point values** | MVC+DRV/r | FTC/TDF+DRV/r | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 396 | 400 | | |
| Units: participants | | | | |
| number (not applicable) | | | | |
| Normal Baseline | 210 | 205 | | |
| Abnormal Baseline | 111 | 101 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Severity of Abnormal Laboratory Values

| End point title | Severity of Abnormal Laboratory Values |
|---|---|

End point description:

Number of participants who had clinically significant laboratory abnormalities of Grade 3 and Grade 4 according to DAIDS. Abnormality incidence of highest grade was reported for a labcode for each individual participant. One participant was not analyzed for laboratory data as the collection date for all lab data was less than the first active therapy date.

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

| **End point values** | MVC+DRV/r | FTC/TDF+DRV/r | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 396 | 401 | | |
| Units: participants | | | | |
| number (not applicable) | | | | |
| Alanine Aminotransferase (ALT) (n=396, 400) | 9 | 6 | | |
| Alkaline Phosphatase (n=396, 400) | 1 | 0 | | |
| Amylase (n=396, 400) | 5 | 13 | | |
| Aspartate Aminotransferase (AST) (n=396, 400) | 11 | 7 | | |
| Blood Urea Nitrogen (BUN) (n=396, 400) | 3 | 5 | | |

| | | | | |
|---|---|---|---|---|
| Calcium (n=396, 400) | 7 | 10 | | |
| Creatine Kinase (n=396, 400) | 18 | 22 | | |
| Hemoglobin (n=396, 400) | 4 | 2 | | |
| LDL Cholesterol (n=396, 400) | 50 | 24 | | |
| Lipase (n=116, 122) | 3 | 10 | | |
| Lymphocytes (Abs) (n=396, 400) | 2 | 2 | | |
| Phosphate (n=396, 400) | 5 | 12 | | |
| Platelets (n=396, 400) | 5 | 1 | | |
| Potassium (n=396, 400) | 3 | 2 | | |
| Sodium (n=396, 400) | 2 | 0 | | |
| Total Bilirubin (n=396, 400) | 3 | 1 | | |
| Total Neutrophils (Abs) (n=396, 400) | 6 | 2 | | |
| Triglycerides (n=396, 400) | 4 | 6 | | |
| Uric Acid (n=396, 400) | 0 | 2 | | |
| White Blood Cell Count (n=396, 400) | 1 | 0 | | |
| Creatinine (n=396, 400) | 0 | 1 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: The relationship between the proportion of participants with plasma HIV-1 RNA <50 copies/mL at the Week 48 and the screening tropism

| | |
|---|---|
| End point title | The relationship between the proportion of participants with plasma HIV-1 RNA <50 copies/mL at the Week 48 and the screening tropism |

End point description:

The relationship of the proportion of participants achieving HIV-1 RNA <50 copies/mL at Week 48 with the screening tropism test for the MVC containing regimen was analyzed. Virologic response for a participant at Week 48 was derived using the FDA's Snapshot MSDF algorithm. Difference in proportions of patients with plasma HIV-1 RNA <50 copies/mL at week 48 between the maraviroc and the emtricitabine/tenofovir treatment arms, with two-sided 95% confidence interval, among patients who are R5 by genotype (including some who were originally randomized to ESTA and are R5 by genotype upon retesting), were calculated via the Maximum Likelihood method. The estimate was adjusted for the screening plasma HIV RNA level (<100,000 vs. ≥100,000 copies/mL) via the Mantel Haenszel (MH) method.

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

End point timeframe:

Week 48

| **End point values** | MVC+DRV/r | FTC/TDF+DRV/r | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 396 | 401 | | |
| Units: proportion of participants | | | | |
| least squares mean (standard error) | 0.8047 (± 0.0238) | 0.8797 (± 0.0187) | | |

## Statistical analyses

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

Statistical analysis description:

The difference in proportions of participants with plasma HIV-1 RNA <50 copies/mL at Week 48 between the [MVC+DRV/r] and the [FTC/TDF+DRV/r] treatment arms, with two-sided 95% confidence interval, is shown for those participants who were R5 by genotype (including all who were originally randomized to ESTA and were R5 by genotype upon retesting), via the maximum likelihood (ML) method.

| | |
|---|---|
| Comparison groups | MVC+DRV/r v FTC/TDF+DRV/r |
| Number of subjects included in analysis | 797 |
| Analysis specification | Pre-specified |
| Analysis type | other[2] |
| Parameter estimate | Other |
| Point estimate | -0.075 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.1343 |
| upper limit | -0.0157 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.0303 |

Notes:

[2] - A statistical model developed for calculating Positive Predictive Values (PPVs) which utilizes all screening tropism assay data (Genotype and ESTA) including screen failures and retesting (enrolled participants only), with clinical response available only for enrolled participants.

## Secondary: Virologic Outcomes at Week 48 using Protocol-Defined Treatment Failure (PDTF).

| End point title | Virologic Outcomes at Week 48 using Protocol-Defined Treatment Failure (PDTF). |
|---|---|

End point description:

Per the protocol, participants who meet the following criteria were regarded as PDTFs requiring a confirmatory plasma HIV-1 RNA determination within 28 days: • Decrease in plasma HIV-1 RNA <1 log10 from baseline after Week 4 unless plasma HIV-1 RNA is <50 copies/mL, or • Plasma HIV-1 RNA >1.0 log10 above the nadir value after Week 4 where the nadir is the lowest plasma HIV-1 RNA concentration, or • Plasma HIV-1 RNA ≥50 copies/mL at any time after Week 24, or • Plasma HIV-1 RNA ≥50 copies/mL after
suppression to <50 copies/mL on two consecutive visits, or • Decrease in plasma HIV-1 RNA ≤2 log10 from baseline on or after Week 12 unless plasma HIV-1 RNA is <400 copies/mL. Decrease in plasma HIV-1 RNA ≤2 log10 from baseline on or after Week 12 unless plasma HIV-1 RNA is <50 copies/mL (before August 30 2012) or <400 copies/mL (amendment after August 30 2012). Evaluable PDTF means that VL >400 cp/mL at the time of failure.

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

End point timeframe:

Week 48

| End point values | MVC+DRV/r | FTC/TDF+DRV/r | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 396 | 401 | | |
| Units: participants | | | | |
| number (not applicable) | | | | |
| Confirmed PDTF | 40 | 13 | | |
| Evaluable PDTF | 17 | 3 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Tropism change between Screening or Baseline and PDTF

| End point title | Tropism change between Screening or Baseline and PDTF |
|---|---|

End point description:

For participants meeting the PDTF criteria, tropism was assessed using the original randomized and alternate assays (ie, both genotype testing and ESTA). Data reported here corresponds to the timepoint at or after PDTF. Number of Evaluable PDTF = Virology Analysis Population (VAP) 'Evaluability' is determined by the on-treatment viral load (≥400 copies/mL at sample time point).

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

End point timeframe:

Baseline to Week 48

| End point values | MVC+DRV/r - Baseline | MVC+DRV/r - Failure | FTC/TDF+DRV/r - Baseline | FTC/TDF+DRV/r - Failure |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 17 | 17 | 3 | 3 |
| Units: participants | | | | |
| number (not applicable) | | | | |
| R5 (Randomized Assay) | 14 | 13 | 2 | 1 |
| NON R5 (Randomized Assay) | 1 | 1 | 0 | 0 |
| NR (Randomized Assay) | 2 | 3 | 1 | 2 |
| R5 (Alternate Assay) | 10 | 10 | 3 | 2 |
| NON R5 (Alternate Assay) | 2 | 3 | 0 | 1 |
| NR (Alternate Assay) | 5 | 4 | 0 | 0 |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with viral resistance to maraviroc (maraviroc treated participants only) in participants meeting PDTF criteria

| End point title | Number of participants with viral resistance to maraviroc (maraviroc treated participants only) in participants meeting PDTF criteria |
|---|---|

End point description:

For participants meeting the PDTF criteria, viral resistance to maraviroc for maraviroc treated participants was assessed in patients with R5 virus at failure. The resistance level is calculated by reference to a laboratory strain of virus that is analyzed in parallel with the clinical isolate to identify 50% inhibitory concentrations (IC50). The maximal percent inhibition is the percent inhibition that is achieved in a titration of the drug at high concentrations when the addition of more drug does not result in increased inhibition. Maximal percent inhibition is obtained in the same way as the titration for IC50, but the key measure is of the plateau height of percent inhibition, where increased concentration of maraviroc does not result in additional inhibition. This is consistent with the virus developing some ability to use maraviroc-bound CCR5 for entry. A significant change in IC50 is not required for this mechanism.

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

End point timeframe:

Week 48

| **End point values** | MVC+DRV/r | FTC/TDF+DRV/r | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 17 | 3 | | |
| Units: participants | | | | |
| number (not applicable) | | | | |
| Not eligible for analysis (failed tropism test) | 4 | 1 | | |
| Not eligible for analysis (non-R5 tropism) | 1 | 1 | | |
| Eligible for analysis (R5 virus using ESTA) | 12 | 1 | | |
| Results reported | 12 | 1 | | |
| Maximal percent inhibition <95% | 0 | 0 | | |
| IC50 FC ≥3.0 | 0 | 0 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with resistance to nucleos(t)ide/nonnucleoside reverse transcriptase inhibitors and protease inhibitors

| End point title | Number of participants with resistance to nucleos(t)ide/nonnucleoside reverse transcriptase inhibitors and protease inhibitors |
|---|---|

End point description:

For participants meeting the PDTF criteria, viral resistance (both genotypic and phenotypic) to nucleoside/nucleotide reverse transcriptase inhibitors (NRTI), non-nucleoside reverse transcriptase inhibitors (NNRTI), and protease inhibitors (PI) were assessed at Baseline and on-treatment. The assessment was performed using the overall (i.e. net) susceptibility score provided using the PhenoSense GT assay. The number of participants with successful assessments were 15/17 for the MVC+DRV/r arm and 3/3 for the FTC/TDF+DRV/r arm.

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

End point timeframe:

Week 48

| End point values | MVC+DRV/r | FTC/TDF+DRV/r | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 15 | 3 | | |
| Units: participants | | | | |
| number (not applicable) | | | | |
| NRTI - All (Baseline, n=15, 3) | 0 | 0 | | |
| NNRTI Delavirdine (Baseline, n=15, 3) | 1 | 0 | | |
| NNRTI Nevirapine (Baseline, n=15, 3) | 1 | 0 | | |
| NNRTI Efavirenz (Baseline, n=15, 3) | 1 | 0 | | |
| PRI - All (Baseline, n=15, 3) | 0 | 0 | | |
| NRTI - All (PDTF, n=15, 3) | 0 | 0 | | |
| NNRTI Delavirdine (PDTF, n=15, 3) | 1 | 0 | | |
| NNRTI Nevirapine (PDTF, n=15, 3) | 1 | 0 | | |
| NNRTI Efavirenz (PDTF, n=15, 3) | 1 | 0 | | |
| PRI - All (PDTF, n=15, 3) | 0 | 0 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Absolute change from Baseline in Immune Cell Function at Week 48: Lymphocyte Marker cluster of differentiation 4

| End point title | Absolute change from Baseline in Immune Cell Function at Week 48: Lymphocyte Marker cluster of differentiation 4 |
|---|---|

End point description:

Absolute change from Baseline in Immune Cell Function at Week 48: Lymphocyte Marker cluster of differentiation 4 (CD4, cell/mm^3). The differences in the magnitude of changes in CD4+ from Baseline to Week 48 for maraviroc versus emtricitabine/tenofovir were compared.

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

End point timeframe:

Baseline, Week 48

| End point values | MVC+DRV/r | FTC/TDF+DRV/r | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 396 | 401 | | |
| Units: cell/mm^3 | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=396, 401) | 382 (± 173.4) | 379.5 (± 170.9) | | |
| Week 48 (n=394, 396) | 576.9 (± 226) | 574.6 (± 232.1) | | |
| Change from Baseline at Week 48 (n=394, 396) | 194.9 (± 175.5) | 194.2 (± 175.8) | | |

### Statistical analyses

| Statistical analysis title | Statistical analysis 1 |
|---|---|
| Statistical analysis description: | |
| Results were from an ANCOVA model with change from Baseline as the response variable and the following fixed effect model terms: Treatment group, Screening plasma HIV RNA concentration, Screening Tropism Assay, Baseline value of the response variable. | |
| Comparison groups | MVC+DRV/r v FTC/TDF+DRV/r |
| Number of subjects included in analysis | 797 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.975 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -24.4 |
| upper limit | 23.6 |

### Secondary: Percent change from Baseline in Immune Cell Function at Week 48: Lymphocyte Activation Marker CD4

| End point title | Percent change from Baseline in Immune Cell Function at Week 48: Lymphocyte Activation Marker CD4 |
|---|---|
| End point description: | |
| The differences in the magnitude of changes in CD4+ from Baseline through Week 48 for maraviroc versus emtricitabine/tenofovir were compared. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 48 | |

| End point values | MVC+DRV/r | FTC/TDF+DRV/r | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 396 | 401 | | |
| Units: Percentage of lymphocytes | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=396, 401) | 24.2 (± 7.9) | 24.5 (± 8.2) | | |
| Week 48 (n=394, 396) | 31.3 (± 8.3) | 33.7 (± 8.6) | | |
| Change from Baseline at Week 48 (n=394, 396) | 7 (± 5.7) | 9.2 (± 6) | | |

### Statistical analyses

| Statistical analysis title | Statistical analysis 1 |
|---|---|
| Statistical analysis description: | |
| Results were from ANCOVA model with change from Baseline as the response variable and the following fixed effect model terms: Treatment group, Screening plasma HIV RNA concentration, Screening Tropism Assay, Baseline value of the response variable. | |
| Comparison groups | MVC+DRV/r v FTC/TDF+DRV/r |
| Number of subjects included in analysis | 797 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -2.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.1 |
| upper limit | -1.5 |

### Secondary: Absolute change from Baseline in Immune Cell Function at Week 48: Lymphocyte Marker cluster of differentiation 8

| End point title | Absolute change from Baseline in Immune Cell Function at Week 48: Lymphocyte Marker cluster of differentiation 8 |
|---|---|
| End point description: | |
| The differences in the magnitude of changes in CD8+ cell counts from baseline through Week 48 for maraviroc versus emtricitabine/tenofovir were compared. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 48 | |

| End point values | MVC+DRV/r | FTC/TDF+DRV/r | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 396 | 401 | | |
| Units: cell/mm^3 | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=396, 401) | 954.4 (± 502.1) | 914.5 (± 473) | | |
| Week 48 (n=394, 396) | 900 (± 508.3) | 751.1 (± 386.7) | | |

| | | | | |
|---|---|---|---|---|
| Change from Baseline at Week 48 (n=394, 396) | -49.9 (± 410.7) | -157.9 (± 444) | | |

**Statistical analyses**

| **Statistical analysis title** | Statistical analysis 1 |
|---|---|
| Comparison groups | MVC+DRV/r v FTC/TDF+DRV/r |
| Number of subjects included in analysis | 797 |
| Analysis specification | Pre-specified |
| Analysis type | other[3] |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 127.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 76.5 |
| upper limit | 178.8 |

Notes:

[3] - Results were from ANCOVA model with change from baseline as the response variable and the following fixed effect model terms: Treatment group, Screening plasma HIV RNA concentration, Screening Tropism Assay, Baseline value of the response variable.

**Secondary: Percent change from Baseline in Immune Cell Function at Week 48: Lymphocyte Activation Marker CD8**

| End point title | Percent change from Baseline in Immune Cell Function at Week 48: Lymphocyte Activation Marker CD8 |
|---|---|

End point description:

The differences in the magnitude of changes in CD8+ cell counts from Baseline through Week 48 for maraviroc versus emtricitabine/tenofovir were compared.

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

End point timeframe:

Baseline, Week 48

| **End point values** | MVC+DRV/r | FTC/TDF+DRV/r | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 396 | 401 | | |
| Units: Percentage of lymphocytes | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=396, 401) | 57 (± 10.7) | 55.8 (± 10.5) | | |
| Week 48 (n=394, 396) | 46 (± 10.4) | 43 (± 10.2) | | |
| Change from Baseline at Week 48 (n=394, 396) | -10.9 (± 7.2) | -12.6 (± 8.1) | | |

## Statistical analyses

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

Statistical analysis description:

Results were from ANCOVA model with change from Baseline as the response variable and the following fixed effect model terms: Treatment group, Screening plasma HIV RNA concentration, Screening Tropism Assay, Baseline value of the response variable.

| | |
|---|---|
| Comparison groups | MVC+DRV/r v FTC/TDF+DRV/r |
| Number of subjects included in analysis | 797 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 2.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.1 |
| upper limit | 3.1 |

## Secondary: Absolute change in CD4+/CD8+ ratio from Baseline to Week 48

| End point title | Absolute change in CD4+/CD8+ ratio from Baseline to Week 48 |
|---|---|

End point description:

The differences in the magnitude of changes in CD4+/CD8+ ratio from Baseline through Weeks 48 for maraviroc versus emtricitabine/tenofovir were compared.

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

End point timeframe:

Baseline, Week 48

| End point values | MVC+DRV/r | FTC/TDF+DRV/r | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 396 | 401 | | |
| Units: Ratio | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=396, 401) | 0.47 (± 0.24) | 0.48 (± 0.25) | | |
| Week 48 (n=394, 396) | 0.75 (± 0.34) | 0.87 (± 0.45) | | |
| Change from Baseline at Week 48 (n=394, 396) | 0.28 (± 0.22) | 0.39 (± 0.34) | | |

### Statistical analyses

| Statistical analysis title | Statistical analysis 1 |
|---|---|
| Statistical analysis description: | |
| Results are from an ANCOVA model with change from Baseline as the response variable and the following fixed effect model terms: Treatment group, Screening plasma HIV RNA concentration, Screening Tropism Assay, Baseline value of the response variable. | |
| Comparison groups | MVC+DRV/r v FTC/TDF+DRV/r |
| Number of subjects included in analysis | 797 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.11 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.15 |
| upper limit | -0.07 |

### Secondary: Changes in Peripheral Fat distribution using Dual Energy X-ray Absorptiometry [DEXA] scan from Baseline and at Week 48

| End point title | Changes in Peripheral Fat distribution using Dual Energy X-ray Absorptiometry [DEXA] scan from Baseline and at Week 48 |
|---|---|
| End point description: | |
| A sub-study was conducted in which the participants underwent whole-body DEXA scans to evaluate peripheral fat tissue estimates for left and right arms, legs, truncal fat mass and truncal lean mass. Truncal abdominal fat were estimated from the DEXA scan field set on the torso. The effects on estimates of fat mass and lean mass were addressed by providing least square mean (LSMs) of change from Baseline. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 48 | |

| End point values | MVC+DRV/r | FTC/TDF+DRV/r | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 52 | 56 | | |
| Units: gram(s) | | | | |
| least squares mean (standard error) | -181.63 (± 569.796) | -257.49 (± 556.884) | | |

### Statistical analyses

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

Statistical analysis description:

Results are from ANCOVA model with change from Baseline as the response variable and the following fixed effect model terms: treatment group, age, race, Screening BMI, and Baseline value of the response variable. Treatment differences are estimated using LS means with factor levels weighted according to overall analysis population proportions.

| | |
|---|---|
| Comparison groups | MVC+DRV/r v FTC/TDF+DRV/r |
| Number of subjects included in analysis | 108 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.8379 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 75.861 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -658.181 |
| upper limit | 809.903 |

### Secondary: Changes in Trunk to Limb fat ratio using DEXA scan from Baseline and at Week 48

| End point title | Changes in Trunk to Limb fat ratio using DEXA scan from Baseline and at Week 48 |
|---|---|

End point description:

A sub-study was conducted in which the participants underwent whole-body DEXA scans to evaluate peripheral fat tissue estimates for left and right arms, legs, truncal fat mass and truncal lean mass. Truncal abdominal fat were estimated from the DEXA scan field set on the torso. The effects on estimates of fat mass and lean mass were addressed by providing LSMs of change from Baseline.

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

End point timeframe:

Week 48

| End point values | MVC+DRV/r | FTC/TDF+DRV/r | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 52 | 56 | | |
| Units: ratio | | | | |
| least squares mean (standard error) | 0.017 (± 0.048) | -0.014 (± 0.048) | | |

### Statistical analyses

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

Statistical analysis description:

Results are from ANCOVA model with change from Baseline as the response variable and the following fixed effect model terms: treatment group, age, race, Screening BMI, and Baseline value of the response variable. Treatment differences are estimated using LS means with factor levels weighted according to overall analysis population proportions.

| | |
|---|---|
| Comparison groups | MVC+DRV/r v FTC/TDF+DRV/r |
| Number of subjects included in analysis | 108 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.3376 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.031 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.033 |
| upper limit | 0.094 |

### Secondary: Changes in bone mineral density (using DEXA scan) from Baseline and at Week 48 - total Hip BMD

| End point title | Changes in bone mineral density (using DEXA scan) from Baseline and at Week 48 - total Hip BMD |
|---|---|

End point description:

Bone mineral density was evaluated by DEXA scan in a subset of participants who consented to these evaluations. The effects on BMD were addressed by providing LSMs of change from baseline bone mineral density of the left total hip as measured by the DEXA scan.

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

End point timeframe:

Week 48

| End point values | MVC+DRV/r | FTC/TDF+DRV/r | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 47 | 57 | | |
| Units: g/cm^2 | | | | |
| least squares mean (standard error) | -0.014 (± 0.005) | -0.028 (± 0.005) | | |

## Statistical analyses

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

Statistical analysis description:

Results are from ANCOVA model with change from Baseline as the response variable and the following fixed effect model terms: treatment group, age, race, Screening BMI, and Baseline value of the response variable. Treatment differences are estimated using LS means with factor levels weighted according to overall analysis population proportions.

| | |
|---|---|
| Comparison groups | MVC+DRV/r v FTC/TDF+DRV/r |
| Number of subjects included in analysis | 104 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0043 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.014 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.004 |
| upper limit | 0.023 |

## Secondary: Changes in bone mineral density (using DEXA scan) from Baseline and at Week 48 - Femoral Neck BMD

| End point title | Changes in bone mineral density (using DEXA scan) from Baseline and at Week 48 - Femoral Neck BMD |
|---|---|

End point description:

Bone mineral density was evaluated by DEXA scan in a subset of participants who consented to these evaluations. The effects on BMD were addressed by providing LSMs of change from Baseline bone mineral density femoral neck as measured by the DEXA scan.

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

End point timeframe:

Week 48

| End point values | MVC+DRV/r | FTC/TDF+DRV/r | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 47 | 57 | | |
| Units: g/cm^2 | | | | |
| least squares mean (standard error) | -0.021 (± 0.007) | -0.029 (± 0.007) | | |

**Statistical analyses**

| **Statistical analysis title** | Statistical analysis 1 |
|---|---|
| Comparison groups | MVC+DRV/r v FTC/TDF+DRV/r |
| Number of subjects included in analysis | 104 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.2273 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.008 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.005 |
| upper limit | 0.022 |

**Secondary: Changes in bone mineral density (using DEXA scan) - AP lumbar spine (L1-L4) BMD**

| End point title | Changes in bone mineral density (using DEXA scan) - AP lumbar spine (L1-L4) BMD |
|---|---|

End point description:

Bone mineral density was evaluated by DEXA scan in a subset of participants who consented to these evaluations. The effects on BMD were addressed by providing LSMs of change from baseline bone mineral density of the lumbar spine (L1-L4) as measured by the DEXA scan.

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

End point timeframe:

Week 48

| **End point values** | MVC+DRV/r | FTC/TDF+DRV/r | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 54 | 60 | | |
| Units: participants | | | | |
| least squares mean (standard error) | -0.02 (± 0.006) | -0.025 (± 0.006) | | |

**Statistical analyses**

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

Statistical analysis description:

Results are from ANCOVA model with change from Baseline as the response variable and the following fixed effect model terms: treatment group, age, race, Screening BMI, and Baseline value of the response variable. Treatment differences are estimated using LS means with factor levels weighted according to overall analysis population proportions.

| | |
|---|---|
| Comparison groups | MVC+DRV/r v FTC/TDF+DRV/r |
| Number of subjects included in analysis | 114 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.4188 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.005 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.007 |
| upper limit | 0.018 |

## Secondary: Change in serum bone turnover markers from Baseline and at Week 48 - Osteocalcin

| End point title | Change in serum bone turnover markers from Baseline and at Week 48 - Osteocalcin |
|---|---|

End point description:

Bone turnover marker, osteocalcin, was collected in the subset of participants participating in the DEXA scan sub-study.

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

End point timeframe:

Week 48

| End point values | MVC+DRV/r | FTC/TDF+DRV/r | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 52 | 61 | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | 5.61 (± 8.02) | 6.77 (± 8.31) | | |

## Statistical analyses

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

Statistical analysis description:

Results are from ANCOVA model with change from Baseline as the response variable and the following fixed effect model terms: treatment group, age, race, Screening BMI, and Baseline value of the response variable. Treatment differences are estimated using LS means with factor levels weighted according to overall analysis population proportions.

| | |
|---|---|
| Comparison groups | MVC+DRV/r v FTC/TDF+DRV/r |
| Number of subjects included in analysis | 113 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.1722 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -2.12 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.17 |
| upper limit | 0.94 |

**Secondary: Change in serum bone turnover markers from Baseline and at Week 48 - Type 1 Collagen Peptide (CTX-1)**

| | |
|---|---|
| End point title | Change in serum bone turnover markers from Baseline and at Week 48 - Type 1 Collagen Peptide (CTX-1) |

End point description:

Bone turnover marker, C-telopeptide of type 1 collagen (CTx), was collected in the subset of participants participating in the DEXA scan sub-study.

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

End point timeframe:

Week 48

| **End point values** | MVC+DRV/r | FTC/TDF+DRV/r | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 53 | 62 | | |
| Units: pg/mL | | | | |
| arithmetic mean (standard deviation) | 121.13 (± 243.03) | 223.52 (± 293.03) | | |

**Statistical analyses**

| **Statistical analysis title** | Statistical analysis 1 |
|---|---|
| Comparison groups | MVC+DRV/r v FTC/TDF+DRV/r |
| Number of subjects included in analysis | 115 |
| Analysis specification | Pre-specified |
| Analysis type | other[4] |
| P-value | = 0.0071 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -126.78 |

| Confidence interval | |
|---|---|
| level | 95 % |
| sides | 2-sided |
| lower limit | -218.34 |
| upper limit | -35.23 |

Notes:

[4] - Results are from an ANCOVA model with change from Baseline as the response variable and the following fixed effect model terms: treatment group, age, race, Screening BMI, Baseline value of the response variable. Treatment differences are estimated using LS means with factor levels weighted according to overall analysis population proportions.

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From the day the first dose of the study medication was administered to 28 days after the last dose of the study medication was administered.

Adverse event reporting additional description:

The same event may appear as both an AE and a SAE. However, what is presented are distinct events. An event may be categorized as serious in one participant and as non-serious in another participant, or one participant may have experienced both a serious and non-serious event during the study.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 17.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | MVC+DRV/r |

Reporting group description:

Participants infected with R5 HIV-1 received oral tablets of Maraviroc 150 mg once daily plus darunavir/ritonavir 800/100 mg once daily plus placebo for emtricitabine/tenofovir once daily.

| | |
|---|---|
| Reporting group title | FTC/TDF+DRV/r |

Reporting group description:

Participants infected with R5 HIV-1 received oral tablets of emtricitabine/tenofovir 200/300 mg once daily plus darunavir/ritonavir 800/100 mg once daily plus placebo for maraviroc once daily.

| Serious adverse events | MVC+DRV/r | FTC/TDF+DRV/r | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 41 / 396 (10.35%) | 40 / 401 (9.98%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Castleman's Disease | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hodgkin's Disease | | | |
| subjects affected / exposed | 2 / 396 (0.51%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Kaposi's Sarcoma | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 396 (0.25%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung Adenocarcinoma | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymphoma | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Testis Cancer | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine Leiomyoma | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Thrombus, Aortic Hepatic Artery | Additional description: Being queried | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Deep Vein Thrombosis | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Surgical and medical procedures | | | |
| Anal Lesion Excision | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Drug Rehabilitation | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 396 (0.00%) | 2 / 401 (0.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Papilloma Excision | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Ectopic Pregnancy | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Chest Pain | | | |
| subjects affected / exposed | 2 / 396 (0.51%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hernia | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Anaphylactic Reaction | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Priapism | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic Obstructive Pulmonary Disease | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary Embolism | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Alcohol Withdrawal Syndrome | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anxiety Disorder | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bipolar I Disorder | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Depression | | | |
| subjects affected / exposed | 2 / 396 (0.51%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Drug Abuse | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Drug Dependence | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Major Depression | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 2 / 401 (0.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mania | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mental Disorder | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Schizophrenia | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Stress | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Suicidal Ideation | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 2 / 401 (0.50%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Suicide Attempt | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 396 (0.25%) | 2 / 401 (0.50%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Amylase Increased | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic Enzyme Increased | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Concussion | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Patella Fracture | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Radius Fracture | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Toxicity To Various Agents | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 2 / 401 (0.50%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Myocardial Infarction | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Pericarditis | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Loss Of Consciousness | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Presyncope | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Iron Deficiency Anaemia | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal Pain | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal Fistula | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal Haemorrhage | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis | | | |
| subjects affected / exposed | 2 / 396 (0.51%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enterocolitis | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal Necrosis | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hiatus Hernia | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Proctitis | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Proctitis Ulcerative | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis Acute | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholelithiasis | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Haematuria | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Intervertebral Disc Protrusion | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rhabdomyolysis | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 2 / 401 (0.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Infections and infestations | | | |
| Acute Hepatitis C | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 2 / 401 (0.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Amoebic Dysentery | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal Abscess | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral Toxoplasmosis | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic Sinusitis | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epididymitis | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye Infection Syphilitic | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatitis A | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes Zoster Infection Neurological | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymph Node Abscess | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neurosyphilis | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pharyngotonsillitis | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia Bacterial | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia Viral | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 396 (0.25%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Shigella Infection | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral Infection | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 0 / 401 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Abnormal Loss Of Weight | | | |
| subjects affected / exposed | 1 / 396 (0.25%) | 3 / 401 (0.75%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 396 (0.00%) | 1 / 401 (0.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | MVC+DRV/r | FTC/TDF+DRV/r | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 355 / 396 (89.65%) | 363 / 401 (90.52%) | |
| Investigations | | | |
| Blood cholesterol increased | | | |
| subjects affected / exposed | 22 / 396 (5.56%) | 10 / 401 (2.49%) | |
| occurrences (all) | 31 | 14 | |
| Low density lipoprotein increased | | | |
| subjects affected / exposed | 22 / 396 (5.56%) | 11 / 401 (2.74%) | |
| occurrences (all) | 35 | 23 | |
| General disorders and administration site conditions | | | |

| | | | |
|---|---|---|---|
| Fatigue | | | |
| subjects affected / exposed | 27 / 396 (6.82%) | 46 / 401 (11.47%) | |
| occurrences (all) | 29 | 49 | |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 9 / 396 (2.27%) | 22 / 401 (5.49%) | |
| occurrences (all) | 9 | 23 | |
| Diarrhoea | | | |
| subjects affected / exposed | 88 / 396 (22.22%) | 135 / 401 (33.67%) | |
| occurrences (all) | 115 | 162 | |
| Nausea | | | |
| subjects affected / exposed | 34 / 396 (8.59%) | 45 / 401 (11.22%) | |
| occurrences (all) | 38 | 49 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 27 / 396 (6.82%) | 30 / 401 (7.48%) | |
| occurrences (all) | 30 | 31 | |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 37 / 396 (9.34%) | 30 / 401 (7.48%) | |
| occurrences (all) | 40 | 41 | |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 26 / 396 (6.57%) | 29 / 401 (7.23%) | |
| occurrences (all) | 29 | 29 | |
| Insomnia | | | |
| subjects affected / exposed | 15 / 396 (3.79%) | 25 / 401 (6.23%) | |
| occurrences (all) | 17 | 26 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 22 / 396 (5.56%) | 23 / 401 (5.74%) | |
| occurrences (all) | 22 | 27 | |
| Headache | | | |
| subjects affected / exposed | 27 / 396 (6.82%) | 47 / 401 (11.72%) | |
| occurrences (all) | 30 | 52 | |
| Infections and infestations | | | |

| | | | |
|---|---|---|---|
| Bronchitis | | | |
| subjects affected / exposed | 25 / 396 (6.31%) | 24 / 401 (5.99%) | |
| occurrences (all) | 32 | 26 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 23 / 396 (5.81%) | 16 / 401 (3.99%) | |
| occurrences (all) | 29 | 16 | |
| Influenza | | | |
| subjects affected / exposed | 22 / 396 (5.56%) | 20 / 401 (4.99%) | |
| occurrences (all) | 24 | 22 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 48 / 396 (12.12%) | 55 / 401 (13.72%) | |
| occurrences (all) | 60 | 80 | |
| Syphilis | | | |
| subjects affected / exposed | 15 / 396 (3.79%) | 23 / 401 (5.74%) | |
| occurrences (all) | 17 | 23 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 40 / 396 (10.10%) | 45 / 401 (11.22%) | |
| occurrences (all) | 54 | 54 | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 12 May 2011 | Protocol amendment 1 provided additional details and clarifications regarding interim analysis. Required additional monitoring of plasma HIV-1 RNA measurements at Week 16 and Week 20 visits in Table 1 (schedule of activities). Described a 2-stage randomization scheme in which both tropism assay and treatment assignment were blinded. Revised the criteria for subjects who were regarded as potential treatment failures. Revised the study protocol to ensure subjects meeting treatment failure criteria undergo a confirmatory plasma HIV-1 RNA assessment within 7-14 days of the initial plasma HIV-1 RNA analysis. Included additional criteria for discontinuation of a subject from the study. Added toxicity management plans for allergic reaction, rash and renal abnormalities. Removed definitions for virologic data analyses previously provided. Updated the structure and content of the study protocol in order to comply with the current Sponsor-approved study protocol template. |
| 14 November 2011 | Protocol amendment 2 revised toxicity management plans for allergic reaction, rash and renal abnormalities. ACTG Grading Severity of Adult Adverse Events with Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events. Version 1.0, December, 2004. Provided introductory text for Siemens HIV-1 Co-receptor Tropism Laboratory Developed Test. Revised one of the potential treatment failure criteria. Provided additional details regarding Virus Tropism Testing. Provided additional details regarding Breaking the Blind for subjects who completed the Week 96 visit prior to locking the database at Week 96. Permitted the provision of study drug after study completion for ethical considerations. Clarified the content and structure of the M-MASRI. Allowed for translation of the Healthcare Resource Utilization Questionnaire (HCRUQ). Replaced glycosylated hemoglobin with insulin in the Fasting Metabolic Assessments in the Schedule of Activities. Omitted Hepatitis B viral load from the Schedule of Activities. Clarified that at the Week 16 and Week 20 visits, only plasma samples were collected for HIV-1 RNA testing throughout the study protocol. Permitted the conduct of the DEXA scan within up to -4 days of the Baseline/Day 1 visit. Updated the structure and content of the study protocol in order to comply with the current Sponsor-approved study protocol template. Clarified the use of stratum adjusted Mantel-Haenszel (MH) method in the analysis of primary and secondary endpoints. Broadened the scope of prohibited medications to include all immunomodulators. Omitted the reference to human genotypic testing to investigate potential MVC toxicities. Clarification and administrative changes. |
| 22 August 2012 | Protocol amendment 3 revised one of the potential treatment failure criteria. Modified sections to report medication errors as adverse events regardless of whether a medication error was accompanied by an AE. Modified to add the dosing instructions and the requirement for the site to contact subjects to review dosing instructions. Modified sections to be compliant with the Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events. Clarified that the EQ 5D instrument was administered by a clinician, nurse or study investigator. Added hematology tests, PT and INR as assessments. Administrative changes were made. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|---|---|---|

| | | |
|---|---|---|
| 15 January 2014 | Even though the study was terminated based on the Data Monitoring Committee (DMC's) recommendation which was accepted by the Sponsor on 04 Oct 2013, the study team remained blinded until the Week 48 database snapshot, which was taken on 15 Jan 2014. The DMC's recommendation was not based on any new drug-related safety events and was based solely on inferior efficacy of the investigational MVC QD, 2 drug regimen arm. This recommendation was made on 27 Sep 2013 and endorsed by the study Sponsor, ViiV Healthcare on 04 Oct 2013. | - |

Notes:

## Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

| |
|---|
| Based on a preliminary review of the 48- week primary clinical efficacy data, the study's external IDMC recommended to early terminate the study due to the inferior efficacy of the MVC+DRV/r arm. So most participants did not reach Week 96. |

Notes: