EU Clinical Trials Register

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	Subject, Investigator

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: