Clinical trial results:
A multicentre, randomised, double-blind, placebo-controlled trial of novel CCR5 antagonist, UK-427,857, in comination with optimised background therapy versus optimised background therapy alone for the treatment of antiretroviral-experienced, non CCR5-tropic and HIV-1 infected subjects

Summary

EudraCT number	2004-001779-20
Trial protocol	SE DE ES BE GB
Global end of trial date	07 April 2009

Results information

Result version number	v1 (current)
This version publication date	01 April 2016
First version publication date	23 July 2015

Trial information

Trial identification

Sponsor protocol code	A4001029

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00098748
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 800-718-1021, 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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 March 2007
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 April 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To confirm that the hypothesis that UK-427,857 added to Optimised Background Therapy (OBT) provides an additional reduction in plasma HIV-1 RNA (Human immunodeficiency virus-1 Ribonucleic Acid) compared to OBT alone, as measured by the difference between each of the two UK-427,857 regimens versus the placebo regimen in the mean changes from baseline in plasma HIV-1 RNA at week 24.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed

Background therapy:

Subjects must have had greater than or equal to (≥3) months of prior treatment with at least 1 agent from 3 of the 4 antiretroviral drug classes.

Evidence for comparator: -

Actual start date of recruitment	30 November 2004
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: 11
Country: Number of subjects enrolled	United States: 125
Country: Number of subjects enrolled	Switzerland: 1
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Canada: 15
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Belgium: 11
Country: Number of subjects enrolled	Germany: 7
Worldwide total number of subjects	186
EEA total number of subjects	34

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)	4
Adults (18-64 years)	181
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Total 232 subjects were screened of whom 190 were randomised to receive treatment from 05 March 2007 to 07 Apr 2009 in 72 centres in 9 countries. Four subjects were randomised, but not treated.

Period 1

Period 1 title	Assigned to Study Treatment
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Maraviroc QD

Arm description:

Maraviroc in combination with optimized background therapy (OBT) (3 to 6 drugs based on treatment history and resistance testing). The 150 mg = maraviroc placebo in the morning and active maraviroc in the evening.

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

Dosage and administration details:

Subjects received Maraviroc 150 mg QD.

Arm title	Maraviroc BID

Arm description:

Maraviroc in combination with OBT (3 to 6 drugs based on treatment history and resistance testing). The 150 mg twice a day (BID) arm = active drug in the morning and evening.

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

Dosage and administration details:

Subjects received Maraviroc 150 mg BID.

Arm title	Placebo

Arm description:

Placebo BID in combination with OBT (3 to 6 drugs based on treatment history and resistance testing). The placebo arm = placebo drug in the morning and evening.

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Placebo matching to Maraviroc BID .

Number of subjects in period 1	Maraviroc QD	Maraviroc BID	Placebo
Started	63	63	64
Completed	63	61	62
Not completed	0	2	2
Randomized, but not treated	-	2	2

Period 2

Period 2 title	Received Study Treatment
Is this the baseline period?	Yes[1]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Maraviroc QD

Arm description:

Maraviroc in combination with optimized background therapy (OBT) (3 to 6 drugs based on treatment history and resistance testing). The 150 mg = maraviroc placebo in the morning and active maraviroc in the evening. Dual-tropic: Virus capable of using both CCR5 and CXCR4 coreceptors for cell entry.

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

Dosage and administration details:

Subjects received Maraviroc 150 mg QD.

Arm title	Maraviroc BID

Arm description:

Maraviroc in combination with OBT (3 to 6 drugs based on treatment history and resistance testing). The 150 mg twice a day (BID) arm = active drug in the morning and evening. Due to 1 placebo subject switched to maraviroc BID, BID = 62 subjects in Adverse event tables.

Arm type	Experimental

Investigational medicinal product name	Maraviroc
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Maraviroc 150 mg BID in combination with OBT.

Arm title	Placebo

Arm description:

Placebo BID in combination with OBT (3 to 6 drugs based on treatment history and resistance testing). The placebo arm = placebo drug in the morning and evening. Due to 1 placebo subject switched to maraviroc BID, Placebo = 61 subjects in Adverse event tables.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received placebo matching to Maraviroc BID in combination with OBT.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Period 2 is the baseline period, since baseline data represents only the subjects who received treatment.

Number of subjects in period 2	Maraviroc QD	Maraviroc BID	Placebo
Started	63	61	62
Dual-tropic Subjects by Phenotype Assay	57	52	58
Completed	15	25	18
Not completed	48	36	44
Death	2	1	2
Adverse event	1	2	5
Unspecified	2	2	6
Lack of efficacy	40	27	27
Subject defaulted	3	4	4

Period 3

Period 3 title	Continued on Open-Label Treatment
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes

Arm title	Maraviroc QD

Arm description:

Maraviroc in combination with optimized background therapy (OBT) (3 to 6 drugs based on treatment history and resistance testing). The 150 mg = maraviroc placebo in the morning and active maraviroc in the evening.

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

Dosage and administration details:

Subjects received Maraviroc 150 mg QD.

Arm title	Maraviroc BID

Arm description:

Maraviroc in combination with OBT (3 to 6 drugs based on treatment history and resistance testing). The 150 mg BID arm = active drug in the morning and evening.

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

Dosage and administration details:

Subjects received Maraviroc 150 mg BID in combination with OBT.

Number of subjects in period 3[2]	Maraviroc QD	Maraviroc BID
Started	15	25
Completed	7	10
Not completed	8	15
Consent withdrawn by subject	-	4
Other reason includes protocol violation	6	7
Adverse event	-	1
Lost to follow-up	1	1
Lack of efficacy	1	2

Notes:

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

Justification: Subjects in placebo group did not received open-label maraviroc due to study failing to reach its primary endpoint at Week 24.

Baseline characteristics

Reporting groups	
Reporting group title	Maraviroc QD
Reporting group description:	
Maraviroc in combination with optimized background therapy (OBT) (3 to 6 drugs based on treatment history and resistance testing). The 150 mg = maraviroc placebo in the morning and active maraviroc in the evening. Dual-tropic: Virus capable of using both CCR5 and CXCR4 coreceptors for cell entry.	
Reporting group title	Maraviroc BID
Reporting group description:	
Maraviroc in combination with OBT (3 to 6 drugs based on treatment history and resistance testing). The 150 mg twice a day (BID) arm = active drug in the morning and evening. Due to 1 placebo subject switched to maraviroc BID, BID = 62 subjects in Adverse event tables.	
Reporting group title	Placebo
Reporting group description:	
Placebo BID in combination with OBT (3 to 6 drugs based on treatment history and resistance testing). The placebo arm = placebo drug in the morning and evening. Due to 1 placebo subject switched to maraviroc BID, Placebo = 61 subjects in Adverse event tables.	

Reporting group values	Maraviroc QD	Maraviroc BID	Placebo
Number of subjects	63	61	62
Age categorical Units: Subjects			
<18 years	2	2	0
Between 18 and 24 years	1	1	1
Between 25 and 34 years	2	3	2
Between 35 and 44 years	30	31	31
Between 45 and 54 years	25	21	20
Between 55 and 64 years	3	3	7
≥65 years	0	0	1
Age continuous Units: years			
arithmetic mean	42.7	42.5	44.6
full range (min-max)	16 to 59	16 to 62	23 to 65
Gender categorical Units: Subjects			
Female	10	6	9
Male	53	55	53

Reporting group values	Total		
Number of subjects	186		
Age categorical Units: Subjects			
<18 years	4		
Between 18 and 24 years	3		
Between 25 and 34 years	7		
Between 35 and 44 years	92		
Between 45 and 54 years	66		
Between 55 and 64 years	13		
≥65 years	1		

Age continuous Units: years arithmetic mean full range (min-max)	- 		
Gender categorical Units: Subjects			
Female	25		
Male	161		

End points

End points reporting groups

Reporting group title	Maraviroc QD

Reporting group description:

Maraviroc in combination with optimized background therapy (OBT) (3 to 6 drugs based on treatment history and resistance testing). The 150 mg = maraviroc placebo in the morning and active maraviroc in the evening.

Reporting group title	Maraviroc BID

Reporting group description:

Maraviroc in combination with OBT (3 to 6 drugs based on treatment history and resistance testing). The 150 mg twice a day (BID) arm = active drug in the morning and evening.

Reporting group title	Placebo

Reporting group description:

Placebo BID in combination with OBT (3 to 6 drugs based on treatment history and resistance testing). The placebo arm = placebo drug in the morning and evening.

Reporting group title	Maraviroc QD

Reporting group description:

Maraviroc in combination with optimized background therapy (OBT) (3 to 6 drugs based on treatment history and resistance testing). The 150 mg = maraviroc placebo in the morning and active maraviroc in the evening. Dual-tropic: Virus capable of using both CCR5 and CXCR4 coreceptors for cell entry.

Reporting group title	Maraviroc BID

Reporting group description:

Maraviroc in combination with OBT (3 to 6 drugs based on treatment history and resistance testing). The 150 mg twice a day (BID) arm = active drug in the morning and evening. Due to 1 placebo subject switched to maraviroc BID, BID = 62 subjects in Adverse event tables.

Reporting group title	Placebo

Reporting group description:

Placebo BID in combination with OBT (3 to 6 drugs based on treatment history and resistance testing). The placebo arm = placebo drug in the morning and evening. Due to 1 placebo subject switched to maraviroc BID, Placebo = 61 subjects in Adverse event tables.

Reporting group title	Maraviroc QD

Reporting group description:

Maraviroc in combination with optimized background therapy (OBT) (3 to 6 drugs based on treatment history and resistance testing). The 150 mg = maraviroc placebo in the morning and active maraviroc in the evening.

Reporting group title	Maraviroc BID

Reporting group description:

Maraviroc in combination with OBT (3 to 6 drugs based on treatment history and resistance testing). The 150 mg BID arm = active drug in the morning and evening.

Primary: Change From Baseline in Human Immunodeficiency Virus (HIV-1) Viral Load (Ribonucleic Acid [RNA])

End point title	Change From Baseline in Human Immunodeficiency Virus (HIV-1) Viral Load (Ribonucleic Acid [RNA])

End point description:

Change from baseline in log 10-transformed plasma viral load (HIV-1 RNA) levels (log 10 copies per milliliter [log10 copies/mL]). Baseline value calculated as average of pre-dose measurements collected at screening, randomization, and baseline visits.Full Analysis Set (FAS)-as treated: all randomized subjects classified as dual-tropic by phenotype assay; received at least 1 dose of study treatment. Missing values: discontinuations (DC) imputed as baseline value (change from baseline=0); missing data imputed as Last Observation Carried Forward (LOCF).

End point type	Primary

End point timeframe:

Baseline to Week 24 and Week 48

End point values	Maraviroc QD	Maraviroc BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	57	52	58	
Units: log10 copies/mL				
arithmetic mean (standard error)				
Week 24	-0.89 (± 0.1706)	-1.194 (± 0.206)	-0.953 (± 0.1795)	
Week 48	-0.604 (± 0.1596)	-1.105 (± 0.2071)	0.839 (± 0.1851)	

Statistical analyses

Statistical analysis title	Maraviroc QD vs. Placebo at Week 24

Statistical analysis description:

Maraviroc (MVC) QD versus placebo (PBO) treatment (TX) difference at Week 24. If upper bound of 97.5% confidence interval is <0, it is concluded that dose is superior to PBO. If upper bound is <0.25, it is concluded that MVC is non-inferior to PBO. Assumption: 79% of subjects are dual-tropic; total N=192 needed to be randomized to get N=150 dual-tropic. Standard deviation=0.8 with 2-sided p-value=0.025: 80% power for TX difference of 0.5 for change from baseline in log10-transformed viral

Comparison groups	Maraviroc QD v Placebo
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	other[1]
Method	ANCOVA
Parameter estimate	Least squares mean
Point estimate	0.055
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.528
upper limit	0.638
Variability estimate	Standard error of the mean
Dispersion value	0.2575

Notes:

[1] - For hypothesis of superiority, if upper bound of 97.5% confidence interval (CI) of TX difference was <0 log10 copies/mL, it was concluded that MVC regimen was superior to PBO meaning that MVC added to Optimized Background Therapy (OBT) provides an additional reduction in plasma HIV-1 RNA compared to OBT alone. If superiority could not be concluded, then a hypothesis of non inferiority was tested. If upper bound of CI is <0.25 log10 copies/mL, noninferiority of MVC regimen to placebo was claimed.

Statistical analysis title	Maraviroc BID vs. Placebo at Week 24

Statistical analysis description:

MVC BID vs PBO treatment difference at Week 24. TX difference adjusted for randomization strata. Bonferroni adjustment for multiple comparisons by use of 2-sided 97.5% CI to maintain alpha=0.05. Negative values for change from baseline=benefit of TX; negative values for MVC vs PBO=advantage of MVC.

Comparison groups	Maraviroc BID v Placebo
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	other
Method	ANCOVA
Parameter estimate	Least squares mean
Point estimate	-0.232
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.829
upper limit	0.364
Variability estimate	Standard error of the mean
Dispersion value	0.2637

Statistical analysis title	Maraviroc QD vs. Placebo at Week 48

Statistical analysis description:

MVC QD vs PBO treatment difference at Week 48. TX difference adjusted for randomization strata. Bonferroni adjustment for multiple comparisons by use of 2-sided 97.5% CI to maintain alpha=0.05. Negative values for change from baseline=benefit of TX; negative values for MVC vs PBO=advantage of MVC.

Comparison groups	Maraviroc QD v Placebo
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	other
Method	ANCOVA
Parameter estimate	Least squares mean
Point estimate	0.229
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.351
upper limit	0.81
Variability estimate	Standard error of the mean
Dispersion value	0.2567

Statistical analysis title	Maraviroc BID vs. Placebo at Week 48

Statistical analysis description:

MVC BID vs PBO treatment difference at Week 48. TX difference adjusted for randomization strata. Bonferroni adjustment for multiple comparisons by use of 2-sided 97.5% CI to maintain alpha=0.05. Negative values for change from baseline=benefit of TX; negative values for MVC vs PBO=advantage of MVC.

Comparison groups	Maraviroc BID v Placebo

Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	other
Method	ANCOVA
Parameter estimate	Least squares mean
Point estimate	-0.261
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.856
upper limit	0.333
Variability estimate	Standard error of the mean
Dispersion value	0.2628

Secondary: Number of Subjects With HIV-1 RNA Levels < 400 Copies/mL

End point title	Number of Subjects With HIV-1 RNA Levels < 400 Copies/mL

End point description:

FAS - as treated dual-tropic subjects. Missing values counted as failures/non-responders (counted as not achieving the stated criterion).

End point type	Secondary

End point timeframe:

Week 24, Week 48

End point values	Maraviroc QD	Maraviroc BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	57	52	58	
Units: subjects				
Week 24	14	16	14	
Week 48	12	16	13	

Statistical analyses

Statistical analysis title	Maraviroc QD vs. Placebo at Week 24

Statistical analysis description:

MVC QD vs PBO treatment difference in proportions at Week 24. The TX difference is weighted (by inverse of the variance) difference in proportions adjusted for randomization strata. Positive values for TX difference favor MVC. CI estimated using the normal approximation to the binomial distribution.

Comparison groups	Placebo v Maraviroc QD

Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	difference in proportions
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.12
upper limit	0.18

Statistical analysis title	Maraviroc BID vs. Placebo at Week 24

Statistical analysis description:

MVC BID vs PBO treatment difference in proportions at Week 24. The TX difference is weighted (by inverse of the variance) difference in proportions adjusted for randomization strata. Positive values for TX difference favor MVC. CI estimated using the normal approximation to the binomial distribution.

Comparison groups	Maraviroc BID v Placebo
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	difference in proportions
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.08
upper limit	0.23

Statistical analysis title	Maraviroc QD vs. Placebo at Week 48

Statistical analysis description:

MVC QD vs PBO treatment difference in proportions at Week 48. The TX difference is weighted (by inverse of the variance) difference in proportions adjusted for randomization strata. Positive values for TX difference favor MVC. CI estimated using the normal approximation to the binomial distribution.

Comparison groups	Maraviroc QD v Placebo
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	difference in proportions
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.12
upper limit	0.17

Statistical analysis title	Maraviroc BID vs. Placebo at Week 48

Statistical analysis description:

MVC BID vs PBO treatment difference in proportions at Week 48. The TX difference is weighted (by inverse of the variance) difference in proportions adjusted for randomization strata. Positive values for TX difference favor MVC. CI estimated using the normal approximation to the binomial distribution.

Comparison groups	Maraviroc BID v Placebo
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	difference in proportions
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.07
upper limit	0.25

Secondary: Number of Subjects With HIV-1 RNA Levels < 400 Copies/mL or at Least 0.5 Log 10-transformed Decrease From Baseline in HIV-1 RNA Levels

End point title	Number of Subjects With HIV-1 RNA Levels < 400 Copies/mL or at Least 0.5 Log 10-transformed Decrease From Baseline in HIV-1 RNA Levels

End point description:

Number of subjects with HIV-1 RNA levels < 400 copies/mL or at least 0.5 log 10-transformed decrease from baseline in HIV-1 RNA levels. Baseline value calculated as average of pre-dose measurements collected at screening, randomization, and baseline visits.FAS-as treated dual-tropic subjects. Missing values counted as failures/non-responders (counted as not achieving the stated criterion).

End point type	Secondary

End point timeframe:

Baseline, Week 24, Week 48

End point values	Maraviroc QD	Maraviroc BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	57	52	58	
Units: subjects				
Week 24	24	25	23	
Week 48	14	22	18	

Statistical analyses

Statistical analysis title	Maraviroc QD vs. Placebo at Week 24

Statistical analysis description:

MVC QD vs PBO treatment difference in proportions at Week 24. The TX difference is weighted (by inverse of the variance) difference in proportions adjusted for randomization strata. Positive values for TX difference favor MVC. CI estimated using the normal approximation to the binomial distribution.

Comparison groups	Maraviroc QD v Placebo

Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	difference in proportions
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	0.2

Statistical analysis title	Maraviroc BID vs. Placebo at Week 24

Statistical analysis description:

MVC BID vs PBO treatment difference in proportions at Week 24. The TX difference is weighted (by inverse of the variance) difference in proportions adjusted for randomization strata. Positive values for TX difference favor MVC. CI estimated using the normal approximation to the binomial distribution.

Comparison groups	Maraviroc BID v Placebo
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	difference in proportions
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.26

Statistical analysis title	Maraviroc QD vs. Placebo at Week 48

Statistical analysis description:

MVC QD vs PBO treatment difference in proportions at Week 48. The TX difference is weighted (by inverse of the variance) difference in proportions adjusted for randomization strata. Positive values for TX difference favor MVC. CI estimated using the normal approximation to the binomial distribution.

Comparison groups	Maraviroc QD v Placebo
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	difference in proportions
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.22
upper limit	0.1

Statistical analysis title	Maraviroc BID vs. Placebo at Week 48

Statistical analysis description:

MVC BID vs PBO treatment difference in proportions at Week 48. The TX difference is weighted (by inverse of the variance) difference in proportions adjusted for randomization strata. Positive values for TX difference favor MVC. CI estimated using the normal approximation to the binomial distribution.

Comparison groups	Maraviroc BID v Placebo
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	difference in proportions
Point estimate	0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.07
upper limit	0.28

Secondary: Number of Subjects With HIV-1 RNA Levels < 400 Copies/mL or at Least 1.0 Log 10-transformed Decrease From Baseline in HIV-1 RNA Levels

End point title	Number of Subjects With HIV-1 RNA Levels < 400 Copies/mL or at Least 1.0 Log 10-transformed Decrease From Baseline in HIV-1 RNA Levels

End point description:

Number of subjects with HIV-1 RNA levels < 400 copies/mL or at least 1.0 log 10-transformed decrease from baseline in HIV-1 RNA levels. Baseline value calculated as average of pre-dose measurements collected at screening, randomization, and baseline visits. FAS-as treated dual-tropic subjects. Missing values counted as failures/non-responders (counted as not achieving the stated criterion).

End point type	Secondary

End point timeframe:

Baseline, Week 24, Week 48

End point values	Maraviroc QD	Maraviroc BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	57	52	58	
Units: subjects				
Week 24	18	23	21	
Week 48	13	20	15	

Statistical analyses

Statistical analysis title	Maraviroc QD vs. Placebo at Week 24

Statistical analysis description:

MVC QD vs PBO treatment difference in proportions at Week 24. The TX difference is weighted (by inverse of the variance) difference in proportions adjusted for randomization strata. Positive values for TX difference favor MVC. CI estimated using the normal approximation to the binomial distribution.

Comparison groups	Maraviroc QD v Placebo

Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	difference in proportions
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.21
upper limit	0.12

Statistical analysis title	Maraviroc BID vs. Placebo at Week 24

Statistical analysis description:

MVC BID vs PBO treatment difference in proportions at Week 24. The TX difference is weighted (by inverse of the variance) difference in proportions adjusted for randomization strata. Positive values for TX difference favor MVC. CI estimated using the normal approximation to the binomial distribution.

Comparison groups	Maraviroc BID v Placebo
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	difference in proportions
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.26

Statistical analysis title	Maraviroc QD vs. Placebo at Week 48

Statistical analysis description:

MVC QD vs PBO treatment difference in proportions at Week 48. The TX difference is weighted (by inverse of the variance) difference in proportions adjusted for randomization strata. Positive values for TX difference favor MVC. CI estimated using the normal approximation to the binomial distribution.

Comparison groups	Maraviroc QD v Placebo
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	difference in proportions
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.18
upper limit	0.13

Statistical analysis title	Maraviroc BID vs. Placebo at Week 48

Statistical analysis description:

MVC BID vs PBO treatment difference in proportions at Week 48. The TX difference is weighted (by inverse of the variance) difference in proportions adjusted for randomization strata. Positive values for TX difference favor MVC. CI estimated using the normal approximation to the binomial distribution.

Comparison groups	Maraviroc BID v Placebo
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	difference in proportions
Point estimate	0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.04
upper limit	0.29

Secondary: Number of Subjects With HIV-1 RNA Levels < 50 Copies/mL

End point title	Number of Subjects With HIV-1 RNA Levels < 50 Copies/mL

End point description:

FAS - as treated dual-tropic subjects. Missing values counted as failures/non-responders (counted as not achieving the stated criterion).

End point type	Secondary

End point timeframe:

Baseline, Week 24, Week 48

End point values	Maraviroc QD	Maraviroc BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	57	52	58	
Units: subjects				
Week 24	12	14	9	
Week 48	10	14	13	

Statistical analyses

Statistical analysis title	Maraviroc QD vs. Placebo at Week 24

Statistical analysis description:

MVC QD vs PBO treatment difference in proportions at Week 24. The TX difference is weighted (by inverse of the variance) difference in proportions adjusted for randomization strata. Positive values for TX difference favor MVC. CI estimated using the normal approximation to the binomial distribution.

Comparison groups	Maraviroc QD v Placebo

Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	difference in proportions
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.07
upper limit	0.2

Statistical analysis title	Maraviroc BID vs. Placebo at Week 24

Statistical analysis description:

MVC BID vs PBO difference in proportions at Week 24. The TX difference is weighted (by inverse of the variance) difference in proportions adjusted for randomization strata. Positive values for TX difference favor MVC. CI estimated using the normal approximation to the binomial distribution.

Comparison groups	Maraviroc BID v Placebo
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	difference in proportions
Point estimate	0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0.26

Statistical analysis title	Maraviroc QD vs. Placebo at Week 48

Statistical analysis description:

MVC QD vs PBO treatment difference in proportions at Week 48. The TX difference is weighted (by inverse of the variance) difference in proportions adjusted for randomization strata. Positive values for TX difference favor MVC. CI estimated using the normal approximation to the binomial distribution.

Comparison groups	Maraviroc QD v Placebo
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	difference in proportions
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.18
upper limit	0.1

Statistical analysis title	Maraviroc BID vs. Placebo at Week 48

Statistical analysis description:

MVC BID vs PBO treatment difference in proportions at Week 48. The TX difference is weighted (by inverse of the variance) difference in proportions adjusted for randomization strata. Positive values for TX difference favor MVC. CI estimated using the normal approximation to the binomial distribution.

Comparison groups	Maraviroc BID v Placebo
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	difference in proportions
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.21

Secondary: Change From Baseline in CD4 Cell Count

End point title	Change From Baseline in CD4 Cell Count

End point description:

Change from baseline in CD4 cell count (measured as cells per microliter [cells/µL]). Baseline value calculated as the average of pre-dose measurements collected at screening, randomization, and baseline visits. FAS - as treated dual-tropic subjects. Placebo N: 4 subjects did not have on-treatment information. Missing data imputed using LOCF.

End point type	Secondary

End point timeframe:

Baseline to Week 24 and Week 48

End point values	Maraviroc QD	Maraviroc BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	57	52	54	
Units: cells/µL				
arithmetic mean (standard error)				
Week 24	59.237 (± 8.9661)	62.651 (± 10.0234)	36.367 (± 8.4477)	
Week 48	65.86 (± 10.822)	78.87 (± 11.566)	51.29 (± 12.523)	

Statistical analyses

Statistical analysis title	Maraviroc QD vs. Placebo at Week 24

Statistical analysis description:

MVC QD vs PBO treatment difference at Week 24. TX difference adjusted for randomization strata. Negative values for change from baseline=benefit of TX; negative values for MVC vs PBO=advantage of MVC.

Comparison groups	Maraviroc QD v Placebo

Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	other
Method	ANCOVA
Parameter estimate	Least squares mean
Point estimate	23.927
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.359
upper limit	49.213
Variability estimate	Standard error of the mean
Dispersion value	12.8025

Statistical analysis title	Maraviroc BID vs. Placebo at Week 24

Statistical analysis description:

MVC BID vs PBO treatment difference at Week 24. TX difference adjusted for randomization strata. Negative values for change from baseline=benefit of TX; negative values for MVC vs PBO=advantage of MVC.

Comparison groups	Maraviroc BID v Placebo
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	other
Method	ANCOVA
Parameter estimate	Least squares mean
Point estimate	26.679
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.869
upper limit	52.49
Variability estimate	Standard error of the mean
Dispersion value	13.0678

Statistical analysis title	Maraviroc QD vs. Placebo at Week 48

Statistical analysis description:

MVC QD vs PBO treatment difference at Week 48. TX difference adjusted for randomization strata. Negative values for change from baseline=benefit of TX; negative values for MVC vs PBO=advantage of MVC.

Comparison groups	Maraviroc QD v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	other
Method	ANCOVA
Parameter estimate	Least squares mean
Point estimate	14.61

Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.8
upper limit	47.03
Variability estimate	Standard error of the mean
Dispersion value	16.412

Statistical analysis title	Maraviroc BID vs. Placebo at Week 48

Statistical analysis description:

MVC BID vs PBO treatment difference at Week 48. TX difference adjusted for randomization strata. Negative values for change from baseline=benefit of TX; negative values for MVC vs PBO=advantage of MVC.

Comparison groups	Placebo v Maraviroc BID
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	other
Method	ANCOVA
Parameter estimate	Least squares mean
Point estimate	27.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.38
upper limit	60.8
Variability estimate	Standard error of the mean
Dispersion value	16.754

Secondary: Change From Baseline in CD8 Cell Count

End point title	Change From Baseline in CD8 Cell Count

End point description:

Change from baseline in CD8 cell count (measured as cells/µL). Baseline value calculated as the average of pre-dose measurements collected at screening, randomization, and baseline visits. FAS - as treated dual-tropic subjects. Placebo N: 4 subjects did not have on-treatment information. Missing data imputed using LOCF.

End point type	Secondary

End point timeframe:

Baseline to Week 24 and Week 48

End point values	Maraviroc QD	Maraviroc BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	57	52	54	
Units: cells/µL				
arithmetic mean (standard error)				
Week 24	391.061 (± 57.0135)	322.683 (± 68.3315)	154.293 (± 46.81)	
Week 48	351.23 (± 54.653)	342.87 (± 72.222)	192.3 (± 62.578)	

Statistical analyses

Statistical analysis title	Maraviroc QD vs. Placebo at Week 24

Statistical analysis description:

MVC QD vs PBO treatment difference at Week 24. TX difference adjusted for randomization strata. Negative values for change from baseline= benefit of TX; negative values for MVC vs PBO=advantage of MVC. TX difference adjusted for randomization strata.

Comparison groups	Maraviroc QD v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	other
Method	ANCOVA
Parameter estimate	Least squares mean
Point estimate	234.499
Confidence interval	
level	95 %
sides	2-sided
lower limit	74.913
upper limit	394.084
Variability estimate	Standard error of the mean
Dispersion value	80.799

Statistical analysis title	Maraviroc BID vs. Placebo at Week 24

Statistical analysis description:

MVC BID vs PBO treatment difference at Week 24. TX difference adjusted for randomization strata. Negative values for change from baseline= benefit of TX; negative values for MVC vs PBO=advantage of MVC. TX difference adjusted for randomization strata.

Comparison groups	Maraviroc BID v Placebo
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	other
Method	ANCOVA
Parameter estimate	Least squares mean
Point estimate	188.817

Confidence interval	
level	95 %
sides	2-sided
lower limit	23.999
upper limit	353.635
Variability estimate	Standard error of the mean
Dispersion value	83.4484

Statistical analysis title	Maraviroc QD vs. Placebo at Week 48

Statistical analysis description:

MVC QD vs PBO treatment difference at Week 48. TX difference adjusted for randomization strata. Negative values for change from baseline= benefit of TX; negative values for MVC vs PBO=advantage of MVC. TX difference adjusted for randomization strata.

Comparison groups	Maraviroc QD v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	other
Method	ANCOVA
Parameter estimate	Least squares mean
Point estimate	155.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.49
upper limit	328.37
Variability estimate	Standard error of the mean
Dispersion value	87.304

Statistical analysis title	Maraviroc BID vs. Placebo at Week 48

Statistical analysis description:

MVC QD vs PBO treatment difference at Week 48. TX difference adjusted for randomization strata. Negative values for change from baseline= benefit of TX; negative values for MVC vs PBO=advantage of MVC. TX difference adjusted for randomization strata.

Comparison groups	Maraviroc BID v Placebo
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	other
Method	ANCOVA
Parameter estimate	Least squares mean
Point estimate	182.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.81
upper limit	361.02
Variability estimate	Standard error of the mean
Dispersion value	90.174

Secondary: Time (50% Quartile Point Estimate) to Virologic Failure

End point title	Time (50% Quartile Point Estimate) to Virologic Failure

End point description:

Time to virologic failure based on observed HIV-1 RNA levels and failure events (death; permanent discontinuation of test drug [perm DC]; lost to follow-up [LTFU]; new anti-retroviral drug added (except background drug change to drug of same class); or on open label for early non-response or rebound). Failure: at Time 0 if level not <400 copies/mL (2 consecutive visits) before event(s) or last available visit; at time of earliest event if level <400 copies/mL (on 2 consecutive visits); failure if level ≥400 copies/mL (2 consecutive visits) or 1 visit ≥400 copies/mL followed by perm DC or LTFU.FAS - as treated dual-tropic subjects; (n)=number of subjects with virologic failure at observation for maraviroc QD, maraviroc BID, and placebo, respectively; Week 48 result values (0.00)=virologic failure at Day 0. Here, "99999" in the upper limit of confidence interval values signifies parameter not estimable (NA).

End point type	Secondary

End point timeframe:

Day 1 through Week 24 and through Week 48

End point values	Maraviroc QD	Maraviroc BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	57	52	58	
Units: days				
median (confidence interval 95%)				
Week 24 (n=35, 23, 29)	88 (59 to 99999)	189 (113 to 189)	100 (60 to 99999)	
Week 48 (n=45, 37, 44)	0 (0 to 0)	0 (0 to 142)	0 (0 to 29)	

Statistical analyses

Statistical analysis title	Maraviroc QD vs. Placebo at Week 24

Statistical analysis description:

MVC QD vs PBO at Week 24. Kaplan-Meier survival estimates. TX difference evaluated by log-rank test.

Comparison groups	Maraviroc QD v Placebo
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7524
Method	Logrank

Statistical analysis title	Maraviroc BID vs. Placebo at Week 24

Statistical analysis description:

MVC BID vs PBO at Week 24. Kaplan-Meier survival estimates. TX difference evaluated by log-rank test.

Comparison groups	Maraviroc BID v Placebo

Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.254
Method	Logrank

Statistical analysis title	Maraviroc QD vs. Placebo at Week 48

Statistical analysis description:

MVC QD vs PBO at Week 48. Kaplan-Meier survival estimates. TX difference evaluated by log-rank test.

Comparison groups	Maraviroc QD v Placebo
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8243
Method	Logrank

Statistical analysis title	Maraviroc BID vs. Placebo at Week 48

Statistical analysis description:

MVC BID vs PBO at Week 48. Kaplan-Meier survival estimates. TX difference evaluated by log-rank test.

Comparison groups	Maraviroc BID v Placebo
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6657
Method	Logrank

Secondary: Change From Baseline in Time Averaged Difference (TAD) in log10 HIV-1 RNA

End point title	Change From Baseline in Time Averaged Difference (TAD) in log10 HIV-1 RNA

End point description:

Change from baseline of TAD in log10 HIV-1 RNA viral load calculated as [AUC of HIV-1 RNA viral load (log10 copies/mL) / time period] - Baseline HIV-1 RNA viral load (log10 copies/mL). Baseline value calculated as the average of pre-dose measurements collected at screening, randomization, and baseline visits.FAS - as treated dual-tropic subjects. Discontinuations prior to time point of analysis imputed as 0.

End point type	Secondary

End point timeframe:

Baseline to Week 24 and Week 48

End point values	Maraviroc QD	Maraviroc BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	57	52	58	
Units: log10 copies/mL				
arithmetic mean (standard error)				
Week 24	-0.85 (± 0.151)	-1.151 (± 0.1895)	-0.926 (± 0.1679)	
Week 48	-0.561 (± 0.1475)	-1.066 (± 0.1962)	-0.776 (± 0.17)	

Statistical analyses

Statistical analysis title	Maraviroc QD vs. Placebo at Week 24
Statistical analysis description:	
MVC QD vs PBO treatment difference at Week 24. TX difference adjusted for randomization strata.	
Comparison groups	Maraviroc QD v Placebo
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	other
Method	ANCOVA
Parameter estimate	Least squares mean
Point estimate	0.069
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.396
upper limit	0.535
Variability estimate	Standard error of the mean
Dispersion value	0.2356

Statistical analysis title	Maraviroc BID vs. Placebo at Week 24
Statistical analysis description:	
MVC BID vs PBO treatment difference at Week 24. TX difference adjusted for randomization strata.	
Comparison groups	Maraviroc BID v Placebo
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	other
Method	ANCOVA
Parameter estimate	Least squares mean
Point estimate	-0.218
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.694
upper limit	0.258
Variability estimate	Standard error of the mean
Dispersion value	0.2413

Statistical analysis title	Maraviroc QD vs. Placebo at Week 48
Statistical analysis description:	
MVC QD vs PBO treatment difference at Week 48. TX difference adjusted for randomization strata.	
Comparison groups	Maraviroc QD v Placebo
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	other
Method	ANCOVA
Parameter estimate	Least squares mean
Point estimate	0.209
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.262
upper limit	0.681
Variability estimate	Standard error of the mean
Dispersion value	0.2388

Statistical analysis title	Maraviroc BID vs. Placebo at Week 48
Statistical analysis description:	
MVC BID vs PBO treatment difference at Week 48. TX difference adjusted for randomization strata.	
Comparison groups	Maraviroc BID v Placebo
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	other
Method	ANCOVA
Parameter estimate	Least squares mean
Point estimate	-0.284
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.767
upper limit	0.199
Variability estimate	Standard error of the mean
Dispersion value	0.2445

Secondary: Number of Subjects Per Genotype and Phenotype at Baseline and at Time of Failure

End point title	Number of Subjects Per Genotype and Phenotype at Baseline and at Time of Failure

End point description:

Number of subjects per genotype and phenotype (tests for presence of non CCR5-tropic HIV-1 and for resistance to reverse transcriptase, protease, and fusion inhibitors) at baseline and at time of failure through Week 48 visit. Sensitivity to drug categorized as 0-1, 2-4, >4; scores defined as 0=resistance,

1=sensitive or susceptible with higher number indicating greater sensitivity or susceptibility. FAS-as treated dual-tropic subjects. Genotype and phenotype at screening and at time of failure were not summarized as planned.

End point type	Secondary

End point timeframe:

Baseline through Week 48

End point values	Maraviroc QD	Maraviroc BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[2]	0[3]	0[4]	
Units: subjects				

Notes:

[2] - Genotype and phenotype at screening and at time of failure were not summarized as planned.

[3] - Genotype and phenotype at screening and at time of failure were not summarized as planned.

[4] - Genotype and phenotype at screening and at time of failure were not summarized as planned.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Per Tropism Status at Screening and at the Time of Treatment Failure (Analysis at Week 24)

End point title	Number of Subjects Per Tropism Status at Screening and at the Time of Treatment Failure (Analysis at Week 24)

End point description:

Number of subjects per Tropism status (CCR5 [R5], CXCR4 [X4], Dual Mixed [DM], or Non-reportable/Non-phenotypable [NR/NP]) at Screening (Scr) and at time of treatment failure (Tx fail). Treatment failure defined as insufficient clinical response. HIV-1 RNA viral load <500 copies/ml categorized as below lower limit of quantification (BLQ). Tropism may have been assessed at either the Screening or Baseline visit. The assessment for time of treatment failure is defined as the last on-treatment assessment. Full Analysis Set-as treated; Subjects with DC prior to timepoint not included; LOCF if no result (viral load too low for analysis).

End point type	Secondary

End point timeframe:

Screening through Week 24

End point values	Maraviroc QD	Maraviroc BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35[5]	24[6]	24[7]	
Units: subjects				
Scr: X4, Tx fail: X4	1	1	1	
Scr: X4, Tx fail: DM	1	1	0	
Scr: DM, Tx fail: R5	1	0	4	
Scr: DM, Tx fail: X4	12	12	2	
Scr: DM, Tx fail: DM	19	9	16	
Scr DM, Tx fail: NR/NP	0	0	1	
Scr DM, Tx fail: BLQ	1	0	0	
Scr NR/NP, Tx fail: NR/NP	0	1	0	

Notes:

[5] - Subjects with TX failure due to insufficient clinical response and had a tropism assessment.

[6] - Subjects with TX failure due to insufficient clinical response and had a tropism assessment.

[7] - Subjects with TX failure due to insufficient clinical response and had a tropism assessment.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Per Tropism Status at Screening and Time of Treatment Failure (Analysis at Week 48)

End point title	Number of Subjects Per Tropism Status at Screening and Time of Treatment Failure (Analysis at Week 48)

End point description:

Number of subjects per Tropism status (CCR5 [R5], CXCR4 [X4], Dual Mixed [DM], or Non-reportable/Non-phenotypable [NR/NP]) at Screening (Scr) and at time of treatment failure (Tx fail). Treatment failure defined as insufficient clinical response. HIV-1 RNA viral load <500 copies/ml categorized as below lower limit of quantification (BLQ). Tropism may have been assessed at either the Screening or Baseline visit. The assessment for time of treatment failure is defined as the last on-treatment assessment.Full Analysis Set-as treated Subjects with DC prior to timepoint not included; LOCF if no result (viral load too low for analysis).

End point type	Secondary

End point timeframe:

Screening through Week 48

End point values	Maraviroc QD	Maraviroc BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	40[8]	27[9]	27[10]	
Units: subjects				
Scr: X4, Tx fail: X4	1	1	1	
Scr: X4, Tx fail: DM	1	1	0	
Scr: DM, Tx fail: R5	1	1	5	
Scr: DM, Tx fail: X4	12	12	2	
Scr: DM, Tx fail: DM	24	10	18	
Scr: DM, Tx fail: NR/NP	0	1	1	
Scr: DM, Tx fail: BLQ	1	0	0	
Scr: NR/NP, Tx fail: NR/NP	0	1	0	

Notes:

[8] - Subjects with TX failure due to insufficient clinical response and had a tropism assessment

[9] - Subjects with TX failure due to insufficient clinical response and had a tropism assessment

[10] - Subjects with TX failure due to insufficient clinical response and had a tropism assessment

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment Failure at Week 24 by Overall Susceptibility Score (OSS) at Screening

End point title	Number of Subjects With Treatment Failure at Week 24 by Overall Susceptibility Score (OSS) at Screening

End point description:

Number of subjects for association between screening resistance and virologic response as determined by treatment failure and OSS at screening. OSS categorized as 0-1, 2-4, >4 (maximum value of 6) and calculated as the sum of the net assessment of in vitro phenotypic and genotypic susceptibility using a binary scoring system (0= reduced susceptibility, 1=susceptible) for each antiretroviral agent in OBT. Higher scores indicate greater susceptibility. Full Analysis Set - as treated dual-tropic subjects. Missing values imputed as LOCF.

End point type	Secondary

End point timeframe:

Screening, Week 24

End point values	Maraviroc QD	Maraviroc BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	57	52	58	
Units: subjects				
Scr score: 0-1	21	12	17	
Scr score: 2-4	35	35	40	
Scr score: missing	1	1	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment Failure at Week 48 by Overall Susceptibility Score (OSS) at Screening

End point title	Number of Subjects With Treatment Failure at Week 48 by Overall Susceptibility Score (OSS) at Screening

End point description:

Number of subjects for association between screening resistance and virologic response as determined by treatment failure and OSS at screening. OSS categorized as 0, 1, 2, or ≥3 (maximum value of 6) and calculated as the sum of the net assessment of in vitro phenotypic and genotypic susceptibility using a binary scoring system (0= reduced susceptibility, 1=susceptible) for each antiretroviral agent in OBT. Higher scores indicate greater susceptibility. Full Analysis Set - as treated dual-tropic subjects. Missing values imputed as LOCF.

End point type	Secondary

End point timeframe:

Screening, Week48

End point values	Maraviroc QD	Maraviroc BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	57	52	58	
Units: subjects				
Scr score: 0	1	2	2	
Scr score: 1	19	11	15	
Scr score: 2	21	14	13	
Scr score: ≥3	15	24	27	

Scr score: missing	1	1	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Acquired Immunodeficiency Syndrome (AIDS)-Defining Opportunistic Illnesses (Analysis at Week 24)

End point title	Number of Subjects With Acquired Immunodeficiency Syndrome (AIDS)-Defining Opportunistic Illnesses (Analysis at Week 24)

End point description:

Number of subjects with AIDS-defining opportunistic illnesses based on investigator classification guided by a predefined list of clinical category C adverse events per center for disease control (CDC) HIV classification system. Includes events occurring up to 7 days after last dose of study drug. Full analysis set - as randomized. Week 48 results reflect subsequent updates to data originally reported at Week 24.

End point type	Secondary

End point timeframe:

Baseline through Week 24

End point values	Maraviroc QD	Maraviroc BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	63[11]	61[12]	62[13]	
Units: subjects				
Candidiasis	0	0	1	
Cytomegalovirus chorioretinitis	1	0	0	
Herpes simplex	1	0	0	
Histoplasmosis	1	0	0	
Mycobacterium avium complex infection	1	0	0	
Oesophageal candidiasis	0	2	0	
Pneumocystis jiroveci pneumonia	3	1	0	
Pneumonia	0	0	1	
Encephalitis	0	0	1	

Notes:

[11] - Number of subjects with Category C Adverse Events

[12] - Number of subjects with Category C Adverse Events

[13] - Number of subjects with Category C Adverse Events

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Acquired Immunodeficiency Syndrome (AIDS)-Defining Opportunistic Illnesses (Analysis at Week 48)

End point title	Number of Subjects With Acquired Immunodeficiency Syndrome (AIDS)-Defining Opportunistic Illnesses (Analysis at

	Week 48)

End point description:

Number of subjects with AIDS-defining opportunistic illnesses based on investigator classification guided by a predefined list of clinical Category C Adverse Events per CDC HIV Classification System. Includes events occurring up to 7 days after last dose of study drug. Full Analysis Set - as randomized. Week 48 results reflect subsequent updates to data originally reported at Week 24.

End point type	Secondary

End point timeframe:

Baseline through Week 48

End point values	Maraviroc QD	Maraviroc BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	63[14]	61[15]	62[16]	
Units: subjects				
Candidiasis	0	1	1	
Cytomegalovirus chorioretinitis	1	0	0	
Histoplasmosis	1	0	0	
Oesophageal candidiasis	0	2	0	
Pneumococcal Sepsis	0	1	0	
Pneumocystis jiroveci pneumonia	3	0	0	
Pneumonia	0	1	0	
Encephalitis	0	0	1	

Notes:

[14] - Number of subjects with Category C Adverse Events

[15] - Number of subjects with Category C Adverse Events

[16] - Number of subjects with Category C Adverse Events

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs/SAEs: recorded from Day 1 up to Week 48. All serious adverse events were reported up to 7 months after Week 48 regardless of duration of follow-up.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Maraviroc QD

Reporting group description:

Maraviroc 150 mg by mouth (PO) once daily (QD) in combination with optimized background therapy (OBT) (3 to 6 drugs based on treatment history and resistance testing). The 150 mg = maraviroc placebo in the morning and active maraviroc in the evening.

Reporting group title	Maraviroc BID

Reporting group description:

Maraviroc 150 mg PO twice a day (BID) in combination with OBT (3 to 6 drugs based on treatment history and resistance testing). The 150 mg BID arm = active drug in the morning and evening.

Reporting group title	Placebo

Reporting group description:

Placebo BID in combination with OBT (3 to 6 drugs based on treatment history and resistance testing). The placebo arm = placebo drug in the morning and evening.

Serious adverse events	Maraviroc QD	Maraviroc BID	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 63 (20.63%)	14 / 62 (22.58%)	13 / 61 (21.31%)
number of deaths (all causes)	2	1	2
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Burkitt’s lymphoma			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung adenocarcinoma			

subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Condition aggravated			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Disease progression			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Fatigue			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	3 / 63 (4.76%)	1 / 62 (1.61%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemothorax			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	2 / 61 (3.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Humerus fracture			

subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Central nervous system lesion			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Movement disorder			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenitis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Ascites			

subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess			

subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis bacterial			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Candida infection			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	0 / 63 (0.00%)	2 / 62 (3.23%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear infection			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Histoplasmosis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Meningitis aseptic			

subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal candidiasis			
subjects affected / exposed	0 / 63 (0.00%)	2 / 62 (3.23%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumococcal sepsis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	3 / 63 (4.76%)	0 / 62 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	3 / 63 (4.76%)	2 / 62 (3.23%)	2 / 61 (3.28%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal abscess			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			

subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	1 / 63 (1.59%)	0 / 62 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Maraviroc QD	Maraviroc BID	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	47 / 63 (74.60%)	51 / 62 (82.26%)	43 / 61 (70.49%)
Investigations			
Weight increased			
subjects affected / exposed	4 / 63 (6.35%)	0 / 62 (0.00%)	0 / 61 (0.00%)
occurrences (all)	4	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	6 / 63 (9.52%)	7 / 62 (11.29%)	3 / 61 (4.92%)
occurrences (all)	6	8	3
Headache			
subjects affected / exposed	13 / 63 (20.63%)	11 / 62 (17.74%)	5 / 61 (8.20%)
occurrences (all)	14	15	5
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 63 (6.35%)	0 / 62 (0.00%)	1 / 61 (1.64%)
occurrences (all)	4	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 63 (0.00%)	2 / 62 (3.23%)	7 / 61 (11.48%)
occurrences (all)	0	2	7
Fatigue			
subjects affected / exposed	9 / 63 (14.29%)	10 / 62 (16.13%)	11 / 61 (18.03%)
occurrences (all)	12	12	12
Injection site reaction			
subjects affected / exposed	7 / 63 (11.11%)	13 / 62 (20.97%)	9 / 61 (14.75%)
occurrences (all)	8	14	9
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	6 / 63 (9.52%)	5 / 62 (8.06%)	1 / 61 (1.64%)
occurrences (all)	6	6	1
Diarrhoea			
subjects affected / exposed	19 / 63 (30.16%)	12 / 62 (19.35%)	13 / 61 (21.31%)
occurrences (all)	24	13	15
Nausea			

subjects affected / exposed	10 / 63 (15.87%)	8 / 62 (12.90%)	12 / 61 (19.67%)
occurrences (all)	12	8	13
Vomiting			
subjects affected / exposed	8 / 63 (12.70%)	3 / 62 (4.84%)	8 / 61 (13.11%)
occurrences (all)	9	4	9
Reproductive system and breast disorders			
Metrorrhagia			
subjects affected / exposed	0 / 63 (0.00%)	1 / 62 (1.61%)	0 / 61 (0.00%)
occurrences (all)	0	1	0
Prostatitis			
subjects affected / exposed	1 / 63 (1.59%)	3 / 62 (4.84%)	0 / 61 (0.00%)
occurrences (all)	1	3	0
Vulvovaginal pruritus			
subjects affected / exposed	0 / 63 (0.00%)	0 / 62 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 63 (11.11%)	6 / 62 (9.68%)	4 / 61 (6.56%)
occurrences (all)	8	6	4
Oropharyngeal pain			
subjects affected / exposed	3 / 63 (4.76%)	4 / 62 (6.45%)	1 / 61 (1.64%)
occurrences (all)	4	5	1
Rhinorrhoea			
subjects affected / exposed	0 / 63 (0.00%)	4 / 62 (6.45%)	0 / 61 (0.00%)
occurrences (all)	0	4	0
Skin and subcutaneous tissue disorders			
Night sweats			
subjects affected / exposed	4 / 63 (6.35%)	3 / 62 (4.84%)	1 / 61 (1.64%)
occurrences (all)	4	3	1
Pruritus			
subjects affected / exposed	2 / 63 (3.17%)	3 / 62 (4.84%)	5 / 61 (8.20%)
occurrences (all)	3	4	8
Rash			
subjects affected / exposed	7 / 63 (11.11%)	6 / 62 (9.68%)	7 / 61 (11.48%)
occurrences (all)	7	6	8
Psychiatric disorders			

Insomnia			
subjects affected / exposed	5 / 63 (7.94%)	5 / 62 (8.06%)	3 / 61 (4.92%)
occurrences (all)	5	5	3
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 63 (4.76%)	4 / 62 (6.45%)	1 / 61 (1.64%)
occurrences (all)	3	4	2
Back pain			
subjects affected / exposed	5 / 63 (7.94%)	8 / 62 (12.90%)	2 / 61 (3.28%)
occurrences (all)	8	9	2
Pain in extremity			
subjects affected / exposed	0 / 63 (0.00%)	6 / 62 (9.68%)	2 / 61 (3.28%)
occurrences (all)	0	6	2
Infections and infestations			
Pyrexia			
subjects affected / exposed	5 / 63 (7.94%)	6 / 62 (9.68%)	4 / 61 (6.56%)
occurrences (all)	5	6	8
Bronchitis			
subjects affected / exposed	4 / 63 (6.35%)	6 / 62 (9.68%)	2 / 61 (3.28%)
occurrences (all)	4	6	2
Herpes simplex			
subjects affected / exposed	2 / 63 (3.17%)	4 / 62 (6.45%)	2 / 61 (3.28%)
occurrences (all)	4	4	2
Influenza			
subjects affected / exposed	1 / 63 (1.59%)	4 / 62 (6.45%)	1 / 61 (1.64%)
occurrences (all)	1	4	1
Nasopharyngitis			
subjects affected / exposed	5 / 63 (7.94%)	2 / 62 (3.23%)	3 / 61 (4.92%)
occurrences (all)	8	2	4
Oral candidiasis			
subjects affected / exposed	1 / 63 (1.59%)	5 / 62 (8.06%)	0 / 61 (0.00%)
occurrences (all)	1	5	0
Pharyngitis			
subjects affected / exposed	1 / 63 (1.59%)	5 / 62 (8.06%)	0 / 61 (0.00%)
occurrences (all)	1	5	0
Sinusitis			

subjects affected / exposed	3 / 63 (4.76%)	6 / 62 (9.68%)	4 / 61 (6.56%)
occurrences (all)	4	9	4
Upper respiratory tract infection			
subjects affected / exposed	5 / 63 (7.94%)	10 / 62 (16.13%)	5 / 61 (8.20%)
occurrences (all)	7	16	6
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 63 (1.59%)	5 / 62 (8.06%)	0 / 61 (0.00%)
occurrences (all)	1	5	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 August 2005	1- Addition of pharmacokinetic data to support the suggested guidance for use of efavirenz with UK-427,857 alone. 2- Upon treatment failure, in addition to a confirmatory plasma HIV-1 RNA sample, the following shall also be collected: a.a plasma sample for HIV-1 co-receptor tropism phenotype as determined by the ViroLogic recombinant virus entry; b.a plasma sample for HIV-1 genotype and phenotype as determined by the ViroLogic PhenoSense GT assay;
20 January 2006	1- Addition of blood sample collection at the Randomization visit. 2- Exclusion of isoniazid use. 3- Exclusion of the initiation of potentially myelosuppressive, neurotoxic, hepatotoxic and/or cytotoxic agents within 60 days prior to randomization. 4- Removal of specific exclusion criteria pertaining to history of cardiovascular and cerebrovascular disease.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported