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PROPRIETARY DRUG NAME® / GENERIC DRUG NAME: Selzentry® / Maraviroc

PROTOCOL NO.: A4001026

PROTOCOL TITLE: A Multicenter, Randomized, Double-Blind, Comparative Trial of a Novel CCR5 Antagonist, UK-427,857, in Combination With Zidovudine/Lamivudine Versus Efavirenz in Combination With Zidovudine/Lamivudine for the Treatment of Antiretroviral-Naive HIV-1 Infected Subjects

Study Centers: One hundred and twenty-seven (127) centers took part in the study and enrolled subjects from 12 countries which included 40 centres in the United States (US) (including Puerto Rico); 17 centres in Canada; 13 centres in South Africa; 10 centres in Australia; 9 centres in Argentina; 8 centres in Italy; 7 centres each in Poland, Switzerland and the United Kingdom; 4 centres each in Belgium and Mexico; 1 centre in the Netherlands. An additional 13 centres received study drug but did not randomize any subjects.

Study Initiation Date, Primary Completion Date and Final Completion Date:
15 November 2004 (First Subject First Visit), 12 December 2006 (Primary completion date for Week 48 cut-off) and 13 December 2012 (Last Subject Last Visit for 5 years)

Phase of Development: Phase 2b/3

Study Objectives:

Primary Objective: To assess whether the antiviral activity (ie, <400/50 human immunodeficiency virus Type-1 ribonucleic acid [HIV-1 RNA] copies/mL at Week 48), of each of 2 doses of maraviroc in combination with zidovudine/lamivudine was non-inferior to a reference regimen of efavirenz plus zidovudine/lamivudine in antiretroviral-naive, chemokine (C-C motif) receptor 5 (CCR5) - tropic HIV-1 infected subjects.

Secondary Objectives:

- To assess whether the antiviral activity (ie, <400/50 HIV-1 RNA copies/mL at Week 24), of each of 2 doses of maraviroc in combination with zidovudine/lamivudine was non-inferior to a reference regimen of efavirenz plus zidovudine/lamivudine in antiretroviral-naive, CCR5-tropic HIV-1 infected subjects.

- To assess whether the antiviral activity (ie, <400/50 HIV-1 RNA copies/mL at Week 96), of each of 2 doses of maraviroc in combination with zidovudine/lamivudine was non-inferior to a reference regimen of efavirenz plus zidovudine/lamivudine in antiretroviral-naive, CCR5-tropic HIV-1 infected subjects.

- To compare the time to loss of virological response through Weeks 48 and 96 for each of the 2 maraviroc regimens versus the efavirenz regimen.

- To compare the reduction of plasma $\log_{10}$ HIV-1 RNA from Baseline through Weeks 24, 48 and 96 for each of the 2 maraviroc regimens versus the efavirenz regimen.

- To compare the differences in the magnitude of changes in cluster of differentiation 4 (CD4) cell counts from Baseline through Weeks 24, 48 and 96 for each of the 2 maraviroc regimens versus the efavirenz regimen.

- To compare the differences in the magnitude of changes in cluster of differentiation 8 (CD8) cell counts from Baseline through Weeks 24, 48 and 96 for each of the 2 maraviroc regimens versus the efavirenz regimen.

- To compare the time-averaged difference (TAD) in $\log_{10}$ HIV-1 RNA at Weeks 24, 48 and 96 for each of the 2 maraviroc regimens versus the efavirenz regimen.

- To assess HIV-1 genotype and phenotype at Baseline and at the time of failure (subjects with HIV-1 RNA >400 copies/mL at any visit after Week 4, or other pre-defined reasons for treatment failure).

- To assess HIV-1 tropism at Baseline and at the time of failure (subjects with viral load >400 copies/mL at any visit after Week 4, or other pre-defined reasons for treatment failure).

- To compare the safety and tolerability of each of the 2 maraviroc regimens versus the efavirenz regimen.

METHODS

Study Design: This was a 96 week, multi-national, multicenter, double-blind, randomized (1:1:1), comparative, non-inferiority Phase 2b/3 hybrid (run-in) study to compare the safety and antiviral activity of maraviroc at 2 different doses versus efavirenz, each in combination with zidovudine/lamivudine in HIV-1 infected subjects over the age of 16 with viral load ≥2000 copies/mL.

Prior to the interim analysis, this study planned to enroll a total of 1071 subjects. Two (2) doses of maraviroc (300 mg once daily [QD] and 300 mg twice daily [BID] were evaluated versus efavirenz (600 mg QD) each taken in combination with zidovudine/lamivudine (300 mg/150 mg BID [Combivir]). Following the interim analysis, the maraviroc 300 mg QD treatment group was discontinued (09 January 2006) on the recommendation of the independent data safety and monitoring board (DSMB), as it failed to meet pre-specified criteria for establishing non-inferiority to efavirenz. As a result, the sample size was reduced to 891 subjects and the study continued with 2 treatment groups: maraviroc 300 mg BID and efavirenz 600 mg QD, each in combination with zidovudine/lamivudine. After the termination of the maraviroc 300 mg QD treatment group, eligible subjects were switched to open-label (OL) phase. An additional supplemental phase was done at approximately 3 month intervals in order

to receive and account for the additional maraviroc drug supplies following the OL phase end-of-study visit.

All subjects underwent genotypic and/or phenotypic testing for the presence of CCR5-tropic HIV-1 prior to the first dose of study drug. The percentage of subjects with undetectable viral load was assessed at Week 48 by the standard and more sensitive methods (<400 copies/mL and <50 copies/mL, respectively). All subjects who received at least 1 dose of study drug were assessed for safety. Study procedures are summarized in Table 1.

Table 1. Time Table of Study Procedures

Procedures	Screening (Day -42 to -28)	Randomization (Day -7 to -4)	Baseline[a] Day 1	Week 2[b]	Weeks 4, 8, 12, 16, 20, 32, 40, 60, 72, 84[b,c]	Weeks 24, 48, 96 or Early Termination[b,d]
Informed consent and eligibility check	X					
Medical history			X			
Physical exam/vital signs			X			X
Targeted physical exam/vital signs					X	
Waist/hip lipodystrophy measurements			X			X
Adverse events			X	X	X	X
Concomitant medications			X	X	X	X
Chemistry, hematology	X	X[e]	X	X	X	X
Fasting metabolic assessment			X			X
12-lead ECG			X			X[f]
Orthostatic blood pressure monitoring	X		X[g]	X		X
PK sampling[h]				X	X	X
Urinalysis			X			X
Hepatitis screen	X					
Hepatitis C virus RNA[i]			X		X	X
CD4/CD8	X		X	X	X	X
Plasma viral load	X	X	X	X	X	X
Pregnancy test[j]	X		X		X	X
Plasma/PBMC/proviral DNA storage[k]			X		X	X
Viral resistance (phenotype, genotype)[l]	X				X[m]	X[n]
Co-receptor tropism (phenotype, genotype)[o]	X		X	X	X[p]	X[n]
Host genotyping			X[q]			
Free T4, thyroid stimulating hormone			X			X
ACTG symptom distress module			X		X[r]	X[c]
CT scan (abdomen and thigh)[s]			X			X
Dispense study medication			X	X[t]	X	X[u]
Assess dosing compliance				X	X	X

Table 1. Time Table of Study Procedures

ACTG = AIDS clinical trials group; AIDS = acquired immune deficiency syndrome; BID = twice daily; CD4 = cluster of differentiation of 4 receptor; CD8 = cluster of differentiation of 8 receptor; CT = computed tomography; DNA = deoxyribonucleic acid; ECG = electrocardiogram; ISOD = in study, off drug; n = number of subjects; PBMC = peripheral blood mononuclear cells; PK = pharmacokinetic; RNA = ribonucleic acid; T4 = thyroxine; V3 = third variable loop.

a. Day 1, prior to dosing.
b. All visits occurred within ±4 days.
c. For subjects who had been discontinued from the study and remained ISOD, the ACTG symptom distress module did not need to be completed following the early termination visit. For those subjects who received open-label maraviroc BID dosing, this module was completed according to the outlined schedule.
d. Subjects who discontinued study drug due to treatment failure or for other reasons were followed per protocol until Week 96.
e. Chemistry panel.
f. For subjects who had been discontinued from the study and remained ISOD, a 12-lead ECG was not required following the early termination visit. For those subjects who received open-label maraviroc BID dosing, this test was performed according to the outlined schedule.
g. Subjects with asymptomatic postural hypotension at the Baseline Visit were monitored for 4 hours following the first dose of study drug.
h. Two (2) 5 mL PK samples taken at least 30 minutes apart were required at Weeks 2 and 48. One (1) 5 mL PK sample was required at other visits through Week 48 only. For subjects who were discontinued from the study and remained ISOD, samples for PK testing were not required after the early termination visit was completed. However, for those subjects who received open-label maraviroc BID dosing, samples were collected according to the outlined schedule.
i. If hepatitis C antibody was positive at Screening, the test was to be performed at Baseline, Weeks 12, 24, 48, and 96 or Early Termination.
j. For women of child bearing potential, serum pregnancy tests were to be performed at Screening, and urine tests at the following visits. A positive urine test was confirmed with a serum test.
k. Plasma aliquots (2 of 1 mL each) were obtained at all timepoints. PBMC, and proviral DNA were stored at Baseline and at Weeks 24, 48, and 96 or upon treatment failure only.
l. Reverse transcriptase inhibitor resistance testing was performed to determine eligibility and gp 160 sequencing.
m. Sample was taken upon treatment failure only, as defined in the study (sample was drawn when the confirmatory plasma viral load sample was collected).
n. Test was performed except at early termination if a treatment failure (sample was drawn when confirmatory viral load sample was collected).
o. Genotype (V3 loop alone or as part of gp 160 sequencing) was performed at Baseline, Weeks 24, 48, and 96 and at treatment failure only.
p. Phenotype was performed at these visits and upon treatment failure as defined in the study (sample was drawn when the confirmatory plasma viral load sample was collected).
q. Test was performed unless prohibited by local regulations.
r. Test was performed at Week 12 only.
s. Test was performed in a subset (target n=300) of subjects from selected centers at Baseline and Week 96 or at Early Termination on or after Wee 48. For subjects who were discontinued from the study and remained ISOD, no additional CT scans were necessary following the early termination visit. However, for those subjects who received open-label maraviroc BID dosing, CT scans were performed according to the outlined schedule.
t. Container was from previous visit.
u. At Week 96 or Early Termination, medication was dispensed to subjects who had completed 96 weeks of therapy and for whom it was medically appropriate to continue or begin therapy with maraviroc.

Number of Subjects (Planned and Analyzed): The study planned to enroll and randomize 1071 subjects in a 1:1:1 ratio; 357 subjects each on maraviroc 300 mg QD, maraviroc 300 mg BID and efavirenz 600 mg QD. After the recommendation by the DSMB; the sample size for the study was planned to be reduced to 891 subjects with 177 subjects in maraviroc 300 mg QD; 357 subjects each on maraviroc 300 mg BID and efavirenz 600 mg QD. New subjects were randomized to 1 of 2 treatment groups; maraviroc 300 mg BID and efavirenz 600 mg QD in a 1:1 ratio.

A total of 917 subjects were randomized to receive treatment (740 to maraviroc 300 mg BID/efavirenz 600 mg QD and 177 to maraviroc 300 mg QD treatment group) including 244 in South Africa, 201 in the US, 101 in Poland, 73 in Canada, 70 in Argentina, 52 in Australia, 49 in UK, 39 in Mexico, 35 in Switzerland, 30 in Italy, 19 in Belgium, 4 in Netherland.

A total of 127 subjects who received maraviroc 300 mg BID participated in the supplemental drug dispensing phase.

Diagnosis and Main Criteria for Inclusion: Male or female subjects, ≥16 years of age, infected with CCR5-tropic HIV-1 with a viral load ≥2000 copies/mL. Subjects could not have received any antiretroviral therapy for >14 days and could not have an active or recent (previous 30 days) opportunistic infection or a suspected primary HIV-1 infection. A negative urine pregnancy test at the Baseline Visit for women of child bearing potential (WOCBP). Effective barrier contraception for WOCBP and males.

Study Treatment: Subjects were randomized to receive either maraviroc with matching placebo for efavirenz tablets or efavirenz with matching placebo for maraviroc tablets, along with zidovudine and lamivudine taken orally with or without food. Subjects were to remain on their randomly assigned treatment (double-blind) for a minimum of 96 weeks unless they discontinued from the study early. Subjects were only to take missed doses if the scheduled dose was not taken within 6 hours of the next planned dose. Zidovudine/lamivudine was administered in OL fashion. No other antiretroviral therapy was allowed while on study drug. Following the DSMB's recommendation to discontinue the maraviroc 300 mg QD treatment group, subjects who had been randomized to this treatment group and who were still receiving double-blind medication, were assessed for eligibility to receive OL maraviroc 300 mg BID and, if appropriate, received this new treatment from 09 January 2006. Table 2 presents the various treatments administered during the study period.

During the supplemental drug dispensing phase, maraviroc 300 mg tablets (to be taken BID) were dispensed to eligible subjects at the OL phase End-of-Study visit and again after 3 months if needed. Maraviroc was provided with zidovudine/lamivudine for centers in South Africa only; in all other countries only maraviroc was provided. Maraviroc and zidovudine/lamivudine, could be taken with or without food. Subjects had to take missed doses only if it was not within 6 hours prior to the next planned dose.

Table 2. Treatments Administered

Group	Doses	Double-Blind Treatments Administered
Dosing to 08 January 2006		
Maraviroc 300 mg QD	Maraviroc 300 mg QD + zidovudine 300 mg BID + lamivudine 150 mg BID	Matching maraviroc placebo in the morning and maraviroc 300 mg + efavirenz placebo in the evening
Maraviroc 300 mg BID	Maraviroc 300 mg BID + zidovudine 300 mg BID + lamivudine 150 mg BID	Maraviroc 300 mg in the morning and evening + efavirenz placebo in the evening
Efavirenz 600 mg QD	Efavirenz 600 mg QD + zidovudine 300 mg BID + lamivudine 150 mg BID	Matching maraviroc placebo in the morning and evening + efavirenz 600 mg in the evening
Dosing From 09 January 2006		
Maraviroc 300 mg BID	Maraviroc 300 mg BID + zidovudine 300 mg BID + lamivudine 150 mg BID	Maraviroc 300 mg in the morning and evening + efavirenz placebo in the evening
Efavirenz 600 mg QD	Efavirenz 600 mg QD + zidovudine 300 mg BID + lamivudine 150 mg BID	Matching maraviroc placebo in the morning and evening + efavirenz 600 mg in the evening
Maraviroc 300 mg BID open-label[a]	Maraviroc 300 mg BID + zidovudine 300 mg BID + lamivudine 150 mg BID	Open-label maraviroc 300 mg in the morning and evening

BID = twice a day; QD = once daily.

a. Subjects previously randomized to the terminated maraviroc 300 mg QD treatment group were assessed for eligibility to receive open-label maraviroc 300 mg BID based upon safety criteria and virological response.

Efficacy Endpoints:

Primary Endpoint: Percentages of subjects with viral load undetectable by the standard and more sensitive methods (<400 copies/mL and <50 copies/mL) at 48 weeks.

Secondary Endpoints:

- Percentage of subjects with HIV-1 RNA levels <400 copies/mL analyzed using logistic regression.
- Percentage of subjects with HIV-1 RNA levels <50 copies/mL analyzed using logistic regression.
- Change from Baseline in $\log_{10}$ transformed HIV-1 RNA levels.
- TAD in $\log_{10}$ transformed HIV-1 RNA levels.
- Change from Baseline in CD4 cell count.
- Change from Baseline in CD8 cell count.
- Time to virological failure.
- Changes in genotype, phenotype, and/or tropism in treatment failures after Week 4.

All secondary variables were analyzed at Weeks 48 and 96.

Safety Evaluations: Adverse event (AE) recording, physical examinations, laboratory tests, vital signs, and 12-lead electrocardiograms were performed at specified intervals throughout the study.

Statistical Methods: Efficacy data up to Week 96 or up to the time of discontinuation (if subjects discontinued prior to Week 96) were analyzed. All endpoints at Week 96 were secondary analyses. Efficacy analyses were performed on the full analysis set (FAS) and per protocol (PP) populations comparing maraviroc 300 mg BID and efavirenz 600 mg QD for each endpoint. The FAS was defined as all randomized subjects who receive at least 1 dose of study medication. The PP analysis set included all randomized subjects who received at least 1 dose of study medication; were treated for at least 14 days or discontinued before this time due to treatment failure; were >80% compliant with randomized treatment; and had no violation of any inclusion or exclusion criteria, which would affect efficacy (such as tropism status).

The As Treated and As Randomized analysis sets were investigated to assess the effect on the results of subjects receiving treatments other than those to which they were randomized. The principal endpoint, which was considered secondary to the primary endpoint at Week 48, was the percentage of subjects with undetectable viral load at Week 96 by the standard and more sensitive methods (<400 copies/mL and <50 copies/mL, respectively). The difference in the percentage of subjects with the specified response was assessed and a 1-sided 97.5% confidence interval (CI; adjusted for the randomisation strata) was calculated for the difference between maraviroc 300 mg BID and efavirenz 600 mg QD. If the lower bound of the CI was above -10%, non-inferiority between maraviroc 300 mg BID and efavirenz 600 mg QD would be concluded. A step down procedure was used with the percentage of subjects with undetectable viral load (<400 copies/mL) tested first. If non-inferiority was demonstrated, then the percentage of subjects with undetectable viral load (<50 copies/mL) was tested. Secondary analyses were performed using the FAS and PP analysis sets where appropriate, with subjects reported according to the treatment they actually received.

The safety analysis set consisted of all randomized subjects who received at least 1 dose of study medication. Subjects were reported in the treatment group for the treatment they actually received.

RESULTS

Subject Disposition and Demography: A total of 1730 subjects were screened and 917 were randomized to receive treatment (740 to maraviroc 300 mg BID/efavirenz 600 mg QD and 177 to maraviroc 300 mg QD treatment group). Of the 740 subjects randomized to receive maraviroc 300 mg BID/efavirenz 600 mg QD, 721 received the study drug (360 to maraviroc 300 mg BID and 361 to efavirenz 600 mg QD). Subject evaluation groups for maraviroc 300 mg BID and efavirenz 600 mg QD groups are summarized in Table 3.

Of the 177 subjects randomized to receive maraviroc 300 mg QD, 174 subjects received maraviroc 300 mg QD. All 174 subjects discontinued from maraviroc 300 mg QD because this treatment arm was discontinued by the Sponsor, and 130 of these subjects continued on to maraviroc 300 mg OL BID. The subject evaluation groups for the subjects who received double blind maraviroc 300 mg QD initially and switched to OL maraviroc 300 mg BID later for 96 weeks is provided in Table 4.

A total of 127 subjects participated in the supplemental drug dispensing phase after the 96 week study period. Only safety was assessed in the supplemental phase.

Table 3. Subject Evaluation Groups (Maraviroc BID/Efavirenz QD)

Number of Subjects	Maraviroc 300 mg BID (N=360) n (%)	Efavirenz 600 mg QD (N=361) n (%)
Treated	360	361
Discontinued	129 (35.8%)	123 (34.1%)
Ongoing at Week 96 cut-off	231 (64.2%)	238 (65.9%)
Evaluated for efficacy		
FAS – As Randomized	360 (100.0%)	361 (100.0%)
FAS – As Treated	360 (100.0%)	361 (100.0%)
PP - As Randomized	323 (89.7%)	318 (88.1%)
PP - As Treated	323 (89.7%)	318 (88.1%)
Analyzed for safety		
AEs	360 (100%)	361 (100%)

AEs = adverse events; BID = twice a day; FAS = full analysis set; N = number of subjects in the treatment group in the indicated population; n = number of subjects in each efficacy population as indicated; PP = per protocol; QD = once daily.

Table 4. Subject Evaluation Groups (Maraviroc Double-Blind and Open-Label Phase)

Number (%) of Subjects	Maraviroc 300 mg QD	Maraviroc 300 mg OL BID
Treated	174	130
Discontinued	174 (100%)	33 (25.4%)
Ongoing at cut-off date[a]	0	97 (74.6%)
Analyzed for safety:		
Adverse events	174 (100.0)	130 (100.0)
Laboratory data	172 (98.9)	130 (100.0)
Vital signs	170 (97.7)	130 (100.0)
ECG	124 (71.3)	122 (93.8)

BID = twice a day; ECG = electrocardiogram; OL = open-label; QD = once a day.
a. Table based on data up to Week 96 cut-off.

Table 5 summarizes for the discontinuations from the study in the subjects maraviroc 300 mg BID group and efavirenz 600 mg QD group respectively. Table 6 summarizes the reasons for discontinuations from the study in the subjects who went on received double-blind maraviroc 300 mg QD and subjected to OL maraviroc 300 mg BID group.

Table 5. Summary of Discontinuations From Study (Maraviroc BID/Efavirenz QD)

	Maraviroc 300 mg BID (N=360) n (%)	Efavirenz 600 mg QD (N=361) n (%)
All	129 (35.8)	123 (34.1)
Subject died[a]	2 (0.6)	2 (0.6)
Related to study drug	70 (19.4)	67 (18.6)
AE[b]	15 (4.2)	44 (12.2)
Lack of efficacy	55 (15.3)	23 (6.4)
Not related to study drug	57 (15.8)	54 (15.0)
Adverse event[b]	7 (1.9)	12 (3.3)
Other reason	14 (3.9)	12 (3.3)
Subject defaulted[c]	31 (8.6)	23 (6.4)

AE = adverse event; ARISg = adverse reaction information system-global; BID = twice a day; N = number of subjects in the treatment group in the indicated population; n = number of subjects discontinued due to indicated reason; QD = once daily.

a. Another subject in the efavirenz 600 mg QD treatment group died within 28 days after discontinuation, which was captured in the ARISg database but not in the clinical database and a further 6 subjects died ≥28 days after discontinuing from the study (4 subjects in the maraviroc 300 mg BID treatment group and 2 subjects in the efavirenz 600 mg QD treatment group). These subjects were captured in the ARISg database, but not the clinical database.

b. Five (5) subjects (1 subject in the maraviroc 300 mg BID treatment group and 4 subjects in the efavirenz 600 mg QD treatment group) were discontinued due to AEs but were not included in this table. This was because the database did not have complete disposition data for these subjects before the Week 96 cut-off. Subject defaulted means no longer willing to participate in the study or lost to follow-up. .

c. Subject defaulted means no longer willing to participate in the study or lost to follow-up. .

Table 6. Summary of Discontinuations From Study (Maraviroc Double-Blind and Open-Label Phase)

	Maraviroc 300 mg QD (N=174) n (%)	Maraviroc 300 mg OL BID (N=130) n (%)
All	174 (100.0%)	33 (25.4%)
Subject died	1 (0.6%)	0
Related to study drug	19 (10.9%)	17 (13.1%)
Adverse event	8 (4.6%)	1 (0.8%)
Lack of efficacy	11 (6.3%)	16 (12.3%)
Not related to study drug	154 (88.5%)	16 (12.3%)
Adverse event	6 (3.4%)	0
Lost to follow-up	5 (2.9%)	2 (1.5%)
Other reason	139 (79.9%)	11 (8.5%)
Subject defaulted[a]	4 (2.3%)	3 (2.3%)

BID = twice a day, N = number of subjects in the treatment group in the indicated population, QD = once a day, OL = open-label.

a. Subject defaulted means subject no longer willing to participate in the study or lost to follow-up.

Demographic characteristics for treated subjects are summarized in Table 7 and Table 8.

Table 7. Summary of Demographic Characteristics (Maraviroc BID/Efavirenz QD)

	Maraviroc 300 mg BID			Efavirenz 600 mg QD		
	Male	**Female**	**All**	**Male**	**Female**	**All**
Number of subjects	256	104	360	259	102	361
Age (years)						
Mean (SD)	36.3 (8.8)	37.4 (11.0)	36.7 (9.4)	38.3 (9.6)	35.3 (10.0)	37.4 (9.8)
Range	(20-60)	(21-69)	(20-69)	(19-77)	(18-65)	(18-77)
Race (n [%])						
White	166 (64.8%)	38 (36.5%)	204 (56.7%)	173 (66.8%)	25 (24.5%)	198 (54.8%)
Black	64 (25.0%)	59 (56.7%)	123 (34.2%)	62 (23.9%)	71 (69.6%)	133 (36.8%)
Asian	6 (2.3%)	0	6 (1.7%)	5 (1.9%)	0	5 (1.4%)
Other	20 (7.8%)	7 (6.7%)	27 (7.5%)	19 (7.3%)	6 (5.9%)	25 (6.9%)
Ethnicity (n [%])						
Hispanic/ Latino	46 (18.0%)	21 (20.2%)	67 (18.6%)	61 (23.6%)	15 (14.7%)	76 (21.1%)
Not Hispanic/ Latino	210 (82.0%)	83 (79.8%)	293 (81.4%)	198 (76.4%)	87 (85.3%)	285 (78.9%)

BID = twice a day; n = number of subjects of the indicated race or ethnicity; SD = standard deviation; QD = once daily.

Table 8. Summary of Demographic Characteristics (Maraviroc Double-Blind Open-Label Phase)

	Maraviroc 300 mg QD			Maraviroc 300 mg OL BID		
	Male	**Female**	**All**	**Male**	**Female**	**All**
Number of subjects	130	44	174	99	31	130
Mean age (range), years	39 (21-70)	35 (20-56)	38 (20-70)	39 (21-70)	35 (20-56)	38 (20-70)
Race, n (%)						
White	108 (83.1%)	18 (40.9%)	126 (72.4%)	81 (81.8%)	15 (48.4%)	96 (73.8%)
Black	14[a] (10.8%)	19 (43.2%)	33 (19.0%)	11 (11.1%)	11 (35.5%)	22 (16.9%)
Asian	1 (0.8%)	4 (9.1%)	5 (2.9%)	0	2 (6.5%)	2 (1.5%)
Other	7[a] (5.4%)	3 (6.8%)	10 (5.7%)	7 (7.1%)	3 (9.7%)	10 (7.7%)
Ethnicity (n [%])						
Hispanic/Latino	22 (16.9%)	10 (22.7%)	32 (18.4%)	16 (16.2%)	9 (29.0%)	25 (19.2%)
Not Hispanic/Latino	108 (83.1%)	34 (77.3%)	142 (81.6%)	83 (83.8%)	22 (71.0%)	105 (80.8%)

BID = twice a day; n = number of subjects of the indicated race or ethnicity; OL = open-label; QD = once daily.
a. One (1) subject's race was changed from Black to other (between the Week 48 and Week 96 cut-off) in the database following query resolution as the study progressed.

Efficacy Results: The analyses at Week 96 were considered secondary to the analyses of the primary endpoint at Week 48.

The percentage of subjects with viral load <400 copies/mL at Week 48 for the FAS – As Treated population was similar in both treatment groups, as summarised in Table 9.

Table 9. Percentage of Subjects With Viral Load <400 copies/mL and <50 copies/mL at Week 48: FAS - As Treated Population (Maraviroc BID/Efavirenz QD)

Parameter	Maraviroc 300 mg BID (N=360)	Efavirenz 600 mg QD (N=361)
Week 48		
<400 copies/mL	70.6% (n=254)	73.1% (n=264)
<50 copies/mL	65.3% (n=235)	69.3% (n=250)

BID = twice a day; N = number of subjects in treatment group; FAS = full analysis set; n = number of subjects with an observation; QD = once daily.

The percentage of subjects with viral load <400 copies/mL and <50 copies/mL at Week 48 for the PP-As Treated population was similar in both treatment groups, as summarized in Table 10.

Table 10. Percentage of Subjects With HIV-1 RNA <400 copies/mL and <50 copies/mL at Week 48: PP - As Treated Population (Maraviroc BID/Efavirenz QD)

Parameter	Maraviroc 300 mg BID	Efavirenz 600 mg QD
Week 48		
<400 copies/mL	75.00% (N=320)* (N=248)** (n=240)	78.27% (N=313)* (N=257)** (n=245)
<50 copies/mL	70.00% (N=320)* (N=248)** (n=224)	74.44% (N=313)* (N=257)** (n=233)

* This is the number of subjects in the treatment group in the indicated population used to calculate the percentage.
** This is the number of subjects with an observation at specified timepoint.
Blinded therapy data only is summarized.
Early Termination visits included within normal visits as per visit windowing.
BID = twice a day; HIV = human immunodeficiency virus; N = number of subjects in treatment group; n = number of subjects with an observation; PP = per protocol set; QD = once daily; RNA = ribonucleic acid.

The percentage of subjects with viral load <400 and <50 copies/mL at Week 96 was 52.9% and 48.3%, respectively, for the FAS (all subjects) and 70.8% and 64.6%, respectively, for the FAS (subjects who entered OL). The percentage of subjects with viral load <400 and <50 copies/mL at Weeks 24, 48, and 96 for the FAS (all subjects and subjects who entered OL) are summarized in Table 11.

Table 11. Subjects With Viral Load <400 and <50 copies/mL at Weeks 48, and 96 (Maraviroc 300 mg QD and Open-Label Phase)

Parameter	Maraviroc 300 mg QD → OL BID All Subjects (N=174)	Maraviroc 300 mg QD → OL BID (Subjects Who Entered OL) (N=130)
Week 48		
<400 copies/mL	61.5% (n=107)	82.3% (n=107)
<50 copies/mL	55.8% (n=97)	74.6% (n=97)

BID = twice a day; N = number of subjects in treatment group in the indicated population used to calculate the percentage; n = number of subjects contributing to the calculation of the percentage; OL = open-label; QD = once daily.

Analysis of the difference in proportion of subjects with viral load <400 copies/mL at Week 48 using the FAS – As Treated population met the pre-defined criteria for non-inferiority as the lower bound of the 1-sided 97.5% CI was above -10% (-9.5%) as shown in Table 12.

Table 12. Summary of Difference in Proportion of Subjects With Viral Load <400 copies/mL and <50 copies/mL at Week 48 (FAS-As Treated Population) (Maraviroc BID Versus Efavirenz QD)

Maraviroc 300 mg BID Versus Efavirenz 600 mg QD	Difference in Proportions[a]	
	Difference in Proportions	Lower Bound of 1-Sided 97.5% CI
Week 48		
Viral Load <400 copies/mL	-0.030	-0.095
Viral Load <50 copies/mL	-0.042	-0.109

BID = twice daily; CI = confidence interval; FAS = full analysis set; QD = once daily.
a. Adjusted for randomisation strata.

Results based on the PP – As Treated analysis sets were consistent with results based on the FAS - As Treated population.

Table 13. Summary of Statistical Analysis: Difference in Proportion of Subjects With HIV-1 RNA <400 copies/mL and <50 copies/mL at Week 48 PP – As Treated Population

Comparison* Maraviroc 300 mg BID Versus Efavirenz 600 mg QD	Difference in Proportions	Lower Bound of 1-Sided 97.5% CI
Week 48		
Viral Load <400 copies/mL	-0.41	-0.105
Viral Load <50 copies/mL	-0.44	-0.112

* The estimate of the difference in proportions has been adjusted for the randomization strata as described below:
Stratum 1: Screening HIV-1 RNA level: <100,000 copies/mL, geographic region: northern hemisphere.
Stratum 2: Screening HIV-1 RNA level: <100,000 copies/mL, geographic region: southern hemisphere.
Stratum 3: Screening HIV-1 RNA level: ≥100,000 copies/mL, geographic region: northern hemisphere.
Stratum 4: Screening HIV-1 RNA level: ≥100,000 copies/mL, geographic region: southern hemisphere.
Missing values classified as failures/non-responders.
BID = twice daily; CI = confidence interval; HIV = human immunodeficiency virus; PP = per protocol; QD = once daily; RNA = ribonucleic acid.

Subjects With Viral Load <400 and <50 copies/mL at Week 48 and Week 96:

Table 14 summarises the logistic regression of viral load <400 copies/mL and <50 copies/mL at Week 48 and Week 96 based on the FAS – As Treated population. Logistic regressions at Week 96 showed that there was no statistically ($p>0.05$) or clinically (odds ratio <1) significant difference between subjects who received maraviroc 300 mg BID and subjects who received efavirenz 600 mg QD.

Table 14. Summary of Statistical Analysis of Proportion of Subjects With Viral Load <400 copies/mL and <50 copies/mL at Week 48 and Week 96 (Logistic Regression): FAS – As Treated Population (Maraviroc BID Versus Efavirenz QD)

Comparison	Logistic Regression		
Maraviroc 300 mg BID vs Efavirenz 600 mg QD	Odds Ratio	95% CI	p-Value
Week 48			
Viral load <400 copies/mL	0.88	0.64, 1.22	0.4485
Viral load <50 copies/mL	0.84	0.61, 1.15	0.2724
Week 96			
Viral load <400 copies/mL	0.88	0.65, 1.19	0.3943
Viral load <50 copies/mL	0.79	0.59, 1.07	0.1289

An odds ratio >1 indicates a beneficial response for subjects in the maraviroc 300 mg BID compared with efavirenz 600 mg QD.
BID = twice a day; CI = confidence interval; FAS = full analysis set; QD = once daily; vs = versus.

Table 15 summarises the logistic regression of viral load <400 copies/mL and <50 copies/mL at Week 48 and Week 96 based on the PP – As Treated population.

Table 15. Summary of Statistical Analysis: Proportion of Subjects With HIV-1 RNA <400 copies/mL and <50 copies/mL at Week 48 and Week 96 (Logistic Regression): PP – As Treated Population

Comparison	Logistic Regression		
Maraviroc 300 mg BID vs Efavirenz 600 mg QD	**Odds Ratio**	**95% CI**	**p-Value**
Week 48			
Viral load <400 copies/mL	0.81	(0.56, 1.18)	0.2796
Viral load <50 copies/mL	0.81	(0.57,1.15)	0.2459
Week 96			
Viral load <400 copies/mL	0.82	(0.59, 1.15)	0.2545
Viral load <50 copies/mL	0.74	(0.53, 1.02)	0.0653

Missing values have been classified as failures/non-responders.
An odds ratio >1 indicates a beneficial response for subjects in the maraviroc 300 mg BID compared with efavirenz 600 mg QD.
BID = twice a day; CI = confidence interval; HIV = human immunodeficiency virus; PP = per protocol; QD = once daily; RNA = ribonucleic acid; vs = versus.

Change From Baseline in Viral Load (log_{10} copies/mL) at Week 48 and Week 96: Change from Baseline in viral load by visit is presented in Table 16. Mean decreases from Baseline in viral load were similar for subjects at all-time points in both the maraviroc 300 mg BID and efavirenz 600 mg QD treatment groups.

Table 16. Change From Baseline in Viral Load: FAS – As Treated Population (Maraviroc BID/Efavirenz QD)

Parameter		Maraviroc 300 mg BID (N=360)	Efavirenz 600 mg QD (N=361)
Viral load at Baseline (log_{10} copies/mL)			
Baseline	n	360	361
	Mean (SD)	4.851 (0.6511)	4.857 (0.6156)
Change from Baseline in Viral Load (log_{10} copies/mL) at:			
Week 48	n	261	274
	Mean (SD)	-3.053 (0.7268)	-3.109 (0.6420)
Week 96	n	234	241
	Mean (SD)	-3.024 (0.7613)	-3.087 (0.6852)

The baseline value is the average of the values from Screening, Randomization and Baseline (Day 1) Visits.
BID = twice a day; FAS = full analysis set; N = number of subjects in the treatment group in the indicated population; n = number of subjects contributing to the summary statistics; QD = once daily; SD = standard deviation.

The statistical analysis of the mean change from Baseline in viral load at Week 48 and Week 96 based on the FAS - As Treated population is summarised in Table 17.

Table 17. Summary of Statistical Analysis of Change From Baseline in Viral Load (log_{10} copies/mL) at Week 48 and Week 96 – FAS – As Treated Population (Maraviroc BID/Efavirenz QD)

Treatment Group	N	Adjusted Mean (SE)	Treatment Difference (Maraviroc-Efavirenz)		
			Estimate (SE)	95% CI	p-Value
Week 48					
Maraviroc 300 mg BID	360	-2.28 (0.08)	0.118	-0.094, 0.329	
Efavirenz 600 mg QD	361	-2.40 (0.08)			
Week 96					
Maraviroc 300 mg BID	360	-1.989 (0.0826)	0.100 (0.1162)	-0.128, 0.328	0.3899
Efavirenz 600 mg QD	361	-2.089 (0.0828)			

The baseline value used in the calculation was the average of the values from Screening, Randomization and Baseline (Day 1) Visits.
Missing values were imputed as the baseline value for subjects who discontinued from blinded therapy.
BID = twice a day; CI = confidence interval; FAS = full analysis set; N = number of subjects in the treatment group in the indicated population; QD = once daily; SE = standard error.

The statistical analysis of the mean change from Baseline in viral load at Week 48 and Week 96 based on the PP - As Treated population is summarised in Table 18.

Table 18. Summary of Statistical Analysis of Change From Baseline in Viral Load (log_{10} copies/mL) at Week 48 and Week 96 – PP – As Treated Population

Treatment Group	N	Adjusted mean (SE)	Treatment Difference (Maraviroc - Efavirenz)		
			Estimate (SE)	95% CI	p-Value
Week 48					
Maraviroc 300 mg BID	320	-2.450 (0.0759)	0.137 (0.1073)	-0.074, 0.348	0.2015
Efavirenz 600 mg QD	313	-2.587 (0.0768)			
Week 96					
Maraviroc 300 mg BID	323	-2.155 (0.0844)	0.129 (0.1190)	-0.105, 0.363	0.2785
Efavirenz 600 mg QD	318	-2.284 (0.0850)			

The baseline value used in the calculation was the average of the predose measurements collected at the Screening Visit, Randomization Visit and Baseline Visit.
Missing values were imputed as the baseline value for subjects who discontinued from blinded therapy. BID = twice a day; CI = confidence interval; PP = per protocol set; N = number of subjects in the treatment group in the indicated population; QD = once daily; SE = standard error.

The mean change from Baseline in viral load at Week 96 was -3.03 log_{10} copies/mL for both the FAS (all subjects) and the FAS (subjects who entered open label). The change from Baseline in viral load (log_{10} copies/mL) at Weeks 48, and 96 for the FAS maraviroc 300 mg QD and OL phase is summarized in Table 19.

Table 19. Change From Baseline in Viral Load at Weeks 48, and 96 (log_{10} copies/mL) (Maraviroc 300 mg QD and Open-Label Phase)

Parameter		Maraviroc 300 mg QD → OL BID (All subjects) N=174	Maraviroc 300 mg QD → OL BID (Subjects Who Entered OL) N=130
Viral load at Baseline (log_{10} copies/mL)			
Baseline	n	174	130
	Mean (SD)	4.90 (0.629)	4.82 (0.590)
Change from Baseline in viral load (log_{10} copies/mL) at:			
Week 48	n	113	113
	Mean (SD)	-2.99 (0.669)	-2.99 (0.669)
Week 96	n	95	95
	Mean (SD)	-3.03 (0.601)	-3.03 (0.601)

The baseline value is the average of the screening, randomization and baseline measurements.
BID = twice daily, N = number of subjects in the treatment group in the indicated population; n = number of subjects contributing to the summary statistics; OL = open-label; QD = once daily; SD = standard deviation.

Time-Averaged Difference: The adjusted means of the TAD in log_{10} transformed viral load from Baseline through Week 96 were similar for subjects in the maraviroc 300 mg BID and efavirenz 600 mg QD treatment groups. A summary for the FAS – as treated population for Week 48 and Week 96 is shown in Table 20.

Table 20. Summary of Statistical Analysis of TAD From Baseline to Week 48 and Week 96 in Viral Load: FAS – As Treated Population (Maraviroc BID / Efavirenz QD)

Treatment Group	N	Adjusted Mean (SE)	Treatment Difference (Maraviroc-Efavirenz)		
			Estimate (SE)	95% CI	p-Value
Week 48					
Maraviroc 300 mg BID	360	-2.15 (0.07)	0.111	-0.086, 0.307	
Efavirenz 600 mg QD	361	-2.26 (0.07)			
Week 96					
Maraviroc 300 mg BID	360	-1.945 (0.0798)	0.089 (0.1121)	-0.131, 0.309	0.4270
Efavirenz 600 mg QD	361	-2.034 (0.0800)			

The baseline value used in the calculation was the average of the values from Screening, Randomization and Baseline (Day 1) Visits.
Discontinuations prior to the time point of analysis were imputed as 0.
BID = twice a day; CI = confidence interval; FAS = full analysis set; N = number of subjects in the treatment group in the indicated population; QD = once daily, SE = standard error; TAD = time-averaged difference.

A summary for the PP – as treated population for Week 48 and Week 96 is shown in Table 21.

Table 21. Summary of Statistical Analysis of TAD From Baseline to Week 48 and Week 96 in Log_{10} Transformed HIV-1 RNA: PP – As Treated Population

Treatment Group	N	Adjusted Mean (SE)	Treatment Difference (Maraviroc-Efavirenz)		
			Estimate (SE)	95% CI	p-Value
Week 48					
Maraviroc 300 mg BID	320	-2.312 (0.0703)	0.129 (0.0994)	(-0.066, 0.325)	0.1932
Efavirenz 600 mg QD	313	-2.442 (0.0711)			
Week 96					
Maraviroc 300 mg BID	323	-2.107 (0.0813)	0.117 (0.1147)	(-0.108, 0.343)	0.3065
Efavirenz 600 mg QD	318	-2.224 (0.0820)			

The baseline value used in the calculation was the average of the values from Screening, Randomization and Baseline (Day 1) Visits.
Discontinuations prior to the time point of analysis were imputed as 0.
BID = twice a day; CI = confidence interval; HIV = human immunodeficiency virus; PP = per protocol; N = number of subjects in the treatment group in the indicated population; QD = once daily; RNA = ribonucleic acid; SE = standard error; TAD = time-averaged difference.

Change in CD4 Cell Count From Baseline Through to Week 48 and Week 96: The change from Baseline in CD4 cell count: FAS – as treated population for Week 96 is shown in Table 22 for maraviroc 300 mg BID and efavirenz 600 mg QD treatment groups and in Table 23 for maraviroc 300 mg QD/OL.

Table 22. Change From Baseline in CD4 Cell Count: FAS – As Treated Population (Maraviroc BID/Efavirenz QD)

Parameter		Maraviroc 300 mg BID[a] (N=360)	Efavirenz 600 mg QD (N=361)
CD4 cell count at Baseline (cells/µL)			
Baseline[b]	n	360	360
	Mean (SD)	264.53 (153.582)	271.87 (133.491)
Change from Baseline in CD4 cell count (cells/µL) at:			
Week 48	n	255	265
	Mean (SD)	192.92 (136.441)	165.39 (119.539)
Week 96	n	232	233
	Mean (SD)	252.54 (149.663)	212.94 (141.670)

BID = twice a day; FAS = full analysis set; CD4 = cluster of differentiation 4 receptor; N = number of subjects in the treatment group in the indicated population; n = number of subjects contributing to the summary statistics; QD = once daily; SD = standard deviation.
a. Change from Baseline through Week 48 in CD4 cell counts differ slightly for the maraviroc treatment group from Week 48 report because the data were revised following query resolution as the study progressed.
b. The baseline value is the average of the values from Screening and Baseline (Day 1) Visits.

Table 23. Change From Baseline in CD4 Cell Count: FAS – As Treated Population (Maraviroc 300 mg QD and Open-Label Phase)

Parameter		Maraviroc 300 mg QD → OL BID (All Subjects) (N=174)	Maraviroc 300 mg QD → OL BID (Subjects Who Entered OL) (N=130)
CD4 cell count at Baseline (cells/μL)			
Baseline	n	174	130
	Mean (SD)	274.0 (175.46)	282.1 (170.67)
Change from Baseline in CD4 cell count (cells/μL) at:			
Week 48	n	110	110
	Mean (SD)	208.7 (232.20)	208.7 (232.20)
Week 96	n	92	92
	Mean (SD)	221.0 (158.79)	221.0 (158.79)

The baseline value is the average of the screening and baseline measurements.
BID = twice a day; FAS = full analysis set; CD4 = cluster of differentiation 4 receptor; N = number of subjects in the treatment group in the indicated population; n = number of subjects contributing to the summary statistics; OL = open-label; QD = once daily; SD = standard deviation.

The change from Baseline in CD4 cell count: PP – as treated population is shown in Table 24.

Table 24. Summary of CD4 Cell Count: PP – As Treated Population

Parameter		Maraviroc 300 mg BID (N=323)	Efavirenz 600 mg QD (N=318)
CD4 cell count at Baseline (cells/μL)			
Baseline	n	323	317
	Mean (SD)	261.87 (145.661)	271.88 (129.062)
Week 48	n	245	254
	Mean (SD)	461.52 (205.479)	435.81 (185.881)
Week 96	n	224	226
	Mean (SD)	523.54 (229.670)	485.98 (196.243)

Each individual subject's baseline value is calculated as the average of the predose measurements collected at the Screening Visit and Baseline Visit.
Early Termination visits included within normal visits as per visit windowing.
BID = twice a day; CD4 = cluster of differentiation 4 receptor; N = number of subjects in the treatment group in the indicated population; n = number of subjects contributing to the summary statistics; PP = per protocol; QD = once daily; SD = standard deviation.

The Summary of statistical analysis of change from Baseline in CD4 cell count (cells/μL) at Week 48 and Week 96: FAS – as treated population is shown in Table 25. At Week 96, the mean difference in CD4 cell count between subjects in the maraviroc 300 mg BID treatment group and subjects in the efavirenz 600 mg QD treatment group was 35.44 cell/μL. The 95% CI excluded 0 indicating a statistically significant increase from Baseline in CD4 cell count for subjects in the maraviroc 300 mg BID treatment group compared with subjects in the efavirenz 600 mg QD treatment group.

Table 25. Summary of Statistical Analysis of Change From Baseline in CD4 Cell Count (cells/µL) at Week 48 and Week 96 – FAS – As Treated Population (Maraviroc BID/Efavirenz QD)

Treatment Group	N	Adjusted Mean (SE)	Treatment Difference (Maraviroc-Efavirenz)		
			Estimate (SE)	95% CI	p-Value
Week 48					
Maraviroc 300 mg BID	352	169.8 (6.9)	26.3	7.0, 45.6	-
Efavirenz 600 mg QD	348	143.5 (7.0)			
Week 96					
Maraviroc 300 mg BID	352	206.90 (8.068)	35.44 (11.419)	13.02, 57.86	0.0020
Efavirenz 600 mg QD	348	171.46 (8.113)			

BID = twice a day; CD4 = cluster of differentiation 4 receptor; CI = confidence interval; FAS = full analysis set; N = number of subjects contributing to the summary statistics; QD = once daily; SE = standard error.

The summary of statistical analysis of change from Baseline in CD4 cell count (cells/µL) at Week 48 and Week 96: PP – as treated population is shown in Table 26.

Table 26. Summary of Statistical Analysis of Change From Baseline in CD4 Cell Count (cells/µL) Through Week 48 and Week 96 – PP – As Treated Population

Treatment	N	Adjusted Mean (SE)	Treatment Difference (Maraviroc-Efavirenz)		
			Estimate (SE)	95% CI	p-Value
Week 48					
Maraviroc 300 mg BID	318	174.48 (7.273)	29.21(10.362)	(8.86, 49.56)	0.0050
Efavirenz 600 mg QD	309	145.27 (7.384)			
Week 96					
Maraviroc 300 mg BID	321	212.26 (8.449)	31.26 (12.014)	(7.67, 54.85)	0.0095
Efavirenz 600 mg QD	314	181.00 (8.551)			

LOCF has been used to impute missing values. Blinded therapy values only have been carried forward.
The baseline value used in the calculation of change from Baseline is the average of the predose measurements collected at the Screening Visit and Baseline Visit.
BID = twice a day; CD4 = cluster of differentiation 4 receptor, CI = confidence interval; LOCF = last observation carried forward; PP = per protocol; N = number of subjects contributing to the summary statistics; QD = once daily; SE = standard error.

Change in CD8 Cell Count From Baseline through to Week 48 and Week 96: The change from Baseline in CD8 cell count: FAS – as treated population for Week 48 and Week 96 is shown in Table 27.

Table 27. Change From Baseline in CD8 Cell Count: FAS – As Treated Population (Maraviroc BID/Efavirenz QD)

Parameter		Maraviroc 300 mg BID[a] (N=360)	Efavirenz 600 mg QD (N=361)
CD8 cell count at Baseline (cells/µL)			
Baseline[b]	n	360	360
	Mean (SD)	938.75 (503.414)	935.78 (476.607)
Change from Baseline in CD8 cell count (cells/µL) at:			
Week 48	n	255	265
	Mean (SD)	23.48 (396.716)	-138.93 (382.546)
Week 96	n	232	233
	Mean (SD)	-1.74 (433.962)	-158.31 (411.368)

BID = twice a day; CD8 = cluster of differentiation 8 receptor; FAS = full analysis set; N = number of subjects in the treatment group in the indicated population; n = number of subjects contributing to the summary statistics; QD = once daily; SD = standard deviation.

a. Change from Baseline through Week 48 in CD8 cell counts differ slightly for the maraviroc treatment group from Week 48 report because the data were revised following query resolution as the study progressed.

b. The baseline value is the average of the values from Screening and Baseline (Day 1) Visits.

The change from Baseline in CD8 cell count: PP – as treated population is shown in Table 28.

Table 28. Summary of Change From Baseline in CD8 Cell Count: PP – As Treated Population

Parameter		Maraviroc 300 mg BID (N=323)	Efavirenz 600 mg QD (N=318)
Week 48	n	245	254
	Mean (SD)	18.41 (400.969)	-145.81 (384.490)
Week 96	n	224	226
	Mean (SD)	-8.05 (437.259)	-160.89 (413.676)

The baseline value used in the calculation of change from Baseline is the average of the predose measurements collected at the Screening Visit and Baseline Visit.
Early Termination visits included within normal visits as per visit windowing.
BID = twice a day; CD8 = cluster of differentiation 8 receptor; N = number of subjects in the treatment group in the indicated population; n = number of subjects contributing to the summary statistics; PP = per protocol; QD = once daily; SD = standard deviation.

The summary of statistical analysis of change from Baseline in CD8 cell count (cells/µL) at Week 48 and Week 96 for FAS – as treated population is shown in Table 29.

Table 29. Summary of Statistical Analysis of Change From Baseline in CD8 Cell Count at Week 48 and Week 96 – FAS – As Treated Population (Maraviroc BID/Efavirenz QD)

Treatment Group	N	Adjusted Mean (SE)	Treatment Difference (Maraviroc-Efavirenz)		
			Estimate (SE)	95% CI	p-Value
Week 48					
Maraviroc 300 mg BID	352	41.81 (17.70)	166.29	117.13, 215.46	-
Efavirenz 600 mg QD	348	-124.48 (17.80)			
Week 96					
Maraviroc 300 mg BID	352	24.53 (18.002)	172.22 (25.471)	122.21, 222.23	<0.0001
Efavirenz 600 mg QD	348	-147.69 (18.105)			

BID = twice a day; CD8 = cluster of differentiation 8 receptor; CI = confidence interval; FAS = full analysis set; N = number of subjects contributing to the summary statistics; QD = once daily; SE = standard error.

The summary of statistical analysis of change from Baseline in CD8 cell count (cells/µL) at Week 48 and Week 96 for PP – as treated population is shown in Table 30.

Table 30. Summary of Statistical Analysis: Change From Baseline Through Week 48 and Week 96 in CD8 Cell Count – PP – As Treated Population

Treatment Group	N	Adjusted Mean (SE)	Treatment Difference (Maraviroc-Efavirenz)		
			Estimate (SE)	95% CI	p-Value
Week 48					
Maraviroc 300 mg BID	318	22.53 (18.132)	164.52 (25.820)	(113.82, 215.23)	<0.0001
Efavirenz 600 mg QD	309	-142.00 (18.411)			
Week 96					
Maraviroc 300 mg BID	321	4.02 (18.333)	159.87 (26.056)	(108.70, 211.03)	<0.0001
Efavirenz 600 mg QD	314	-155.84 (18.555)			

LOCF has been used to impute missing values. Blinded therapy values only have been carried forward.
The baseline value used in the calculation of change from Baseline is the average of the predose measurements collected at the Screening Visit and Baseline Visit.
BID = twice a day; CD8 = cluster of differentiation 8 receptor; CI = confidence interval; LOCF = last observation carried forward; PP = per protocol; N = number of subjects contributing to the summary statistics; QD = once daily; SE = standard error.

Time to Failure: The statistical analysis of the time to treatment failure showed that the 95% CI for the hazard ratio included 1, indicating that there was a benefit for subjects in the efavirenz 600 mg QD treatment group. No difference in the time to virologic failure was observed between subjects in the maraviroc 300 mg BID treatment group and subjects in the efavirenz 600 mg QD treatment group. A Summary of the analysis of time to failure is shown in Table 31.

Table 31. Summary of Statistical Analysis of Time to Failure (Maraviroc BID/Efavirenz QD)

Comparison	Log-Rank Test			Cox's Proportion Hazards	
Maraviroc 300 mg BID vs Efavirenz 600 mg QD	**Log-Rank**	**χ^2**	**p-Value**	**Hazard Ratio**	**95% CI**
Time to Virologic Failure (<400 copies/mL)					
Week 48	3.77	0.29	0.5874	1.10	0.83, 1.45
Week 96	5.7379	0.4965	0.4811	1.10	0.86, 1.40
Time to Treatment Failure					
Week 48	12.83	10.39	0.0013	2.39	1.40, 4.07
Week 96	17.0302	13.3952	0.0003	2.26	1.43,3.55

Any visits with no data were excluded for the calculation of the time to treatment failure and the time to virologic failure.
BID = twice a day; CI = confidence interval; QD = once daily; vs = versus.

Virus Resistance and Tropism: At the time of treatment failure 33 (60.0%) subjects in the maraviroc 300 mg BID treatment group and 8 (34.8%) subjects in the efavirenz 600 mg QD treatment group had virus with genotypic and phenotypic evidence of resistance to zidovudine/lamivudine as shown in Table 32. One (1) subject (1.8%) in the maraviroc 300 mg BID treatment group and 14 (60.9%) subjects in the efavirenz 600 mg QD treatment group had virus with genotypic evidence of drug resistance to efavirenz.

Table 32. Summary of Type of NRTI - Associated Mutation at Time of Treatment Failure or Discontinuation (Maraviroc BID/Efavirenz QD)

Mutation	Maraviroc 300 mg BID (N=55) n (%)	Efavirenz 600 mg QD (N=23) n (%)
Time of Treatment Failure		
Any zidovudine/ lamivudine mutation	33 (60.0)	8 (34.8)
Any TAM[a]	6 (10.9)	2 (8.7)
K65R	1 (1.8)	0
M184V/I	33 (60.0)	8 (34.8)
Other NRTI mutation	1 (1.8)	0
No mutation	12 (21.8)	11 (47.8)
NR/Missing	10 (18.2)	4 (17.4)
Time of Treatment Discontinuation		
Any zidovudine/ lamivudine mutation	40 (31.0)	8 (6.5)
Any TAM[a]	6 (4.7)	2 (1.6)
K65R	1 (0.8)	0
M184V/I	40 (31.0)	8 (6.5)
Other NRTI mutation	1 (0.8)	0
No mutation	28 (21.7)	26 (21.1)
NR/Missing	61 (47.3)	89 (72.4)

BID = Twice daily; K65R = lamivudine mutation; M184V/I = lamivudine mutation; N = number of subjects with treatment failure due to insufficient clinical response or number of discontinued subjects; n = number of subjects with indicated NRTI-associated mutation at time of treatment failure or discontinuation; NR = non-reportable; NRTI = nucleoside/nucleotide reverse transcriptase inhibitor; TAM = thymidine analogue-associated mutation; QD = once daily.

a. Any TAM: M41L, D67N, K70R, L210W, T215Y/F, K219Q/E.

A total of 27 subjects in the FAS (all subjects) and 16 subjects in the FAS (subjects who entered OL) had treatment failure due to insufficient clinical response. At time of treatment failure, 20 of 27 subjects (74.1%) in the FAS (all subjects) and 13 of 16 subjects (81.3%) in the FAS (subjects who entered OL) had virus with genotypic evidence of drug resistance to lamivudine. A total of 77 subjects in the FAS (all subjects) and 33 subjects in the FAS (subjects who entered OL) discontinued study treatment. At time of discontinuation, 31 of 77 subjects (40.3%) in the FAS (all subjects) and 19 of 33 subjects (57.6%) in the FAS (subjects who entered open label) had virus with genotypic evidence of drug resistance to lamivudine. The summary of type of NRTI associated mutations at time of treatment failure or discontinuation for double-blind/OL phase is shown in Table 33.

Table 33. Summary of Type of NRTI Associated Mutations at Time of Treatment Failure or Discontinuation (Double-Blind and Open-Label Phase)

Mutations at Time of Treatment Failure or Discontinuation	Maraviroc 300 mg QD → OL BID (All Subjects) N=174	Maraviroc 300 mg QD → OL BID (Subjects Who Entered OL) N=130
Time of Treatment Failure		
n[a]	27	16
Any zidovudine/lamivudine mutations	20 (74.1%)	13 (81.3%)
Any TAM[c]	3 (11.1%)	3 (18.8%)
K65R	0	0
M184V/I	20 (74.1%)	13 (81.3%)
Any other NRTI mutations	0	0
Mutation absent	4 (14.8%)	1 (6.3%)
Time of Treatment Discontinuation		
n[b]	77	33
Any zidovudine/lamivudine mutations	31 (40.3%)	19 (57.6%)
Any TAM[c]	4 (5.2%)	3 (9.1%)
K65R	0	0
M184V/I	31 (40.3%)	19 (57.6%)
Any other NRTI mutations	0	0
Mutation absent	10 (13.0%)	3 (9.1%)

BID = twice daily; OL = open-label; K65R = lamivudine mutation; M184V/I = lamivudine mutation.
N = total number of subjects; NRTI = nucleoside/nucleotide reverse transcriptase inhibitor; QD = once daily; TAM = thymidine analogue-associated mutation.
a. Number of subjects with treatment failure due to insufficient clinical response.
b. Number of discontinued subjects.
c. Any TAM: M41L, D67N, K70R, L210W, T215Y/F, K219Q/E.

The changes in tropism between Baseline and time of treatment failure or discontinuation for OL phase is summarized in Table 34 and for double-blind/OL phase is summarized in Table 35.

Table 34. Change in Tropism Result Between Baseline and Time of Treatment Failure

Treatment Group	Tropism at Baseline[a]	Tropism at Time of Treatment Failure or Discontinuation[b, c]			
		CCR5 n (%)	CXCR4 n (%)	Dual/Mixed n (%)	NR/NP n (%)
Time of Treatment Failure					
Total population	CCR5	24 (31.17)	1 (1.30)	11 (14.29)	12 (15.58)
N=77[d]	Dual/mixed	2 (2.60)	2 (2.60)	4 (5.19)	0
	NR/NP	1 (1.30)	0	0	1 (1.30)
Maraviroc 300 mg BID	CCR5	14 (25.93)	1 (1.85)	11 (20.37)	7 (12.96)
N=54[e]	Dual/mixed	1 (1.85)	2 (3.70)	4 (7.41)	0
	NR/NP	1 (1.85)	0	0	1 (1.85)
Efavirenz 600 mg QD	CCR5	10 (43.48)	0	0	5 (21.74)
N=23[f]	Dual/mixed	1 (4.35)	0	0	0
	NR/NP	0	0	0	0
Time of Discontinuation					
Total population	CCR5	45 (18.07)	1 (0.40)	13 (5.22)	17 (6.83)
N=249[g]	Dual/mixed	2 (0.80)	2 (0.80)	7 (2.81)	1 (0.40)
	NR/NP	1 (0.40)	0	0	1 (0.40)
Maraviroc 300 mg BID	CCR5	27 (21.26)	1 (0.79)	13 (10.24)	10 (7.87)
N=127[h]	Dual/mixed	1 (0.79)	2 (1.57)	6 (4.72)	0
	NR/NP	1 (0.79)	0	0	1 (0.79)
Efavirenz 600 mg QD	CCR5	18 (14.75)	0	0	7 (5.74)
N=122[i]	Dual/mixed	1 (0.82)	0	1 (0.82)	1 (0.82)
	NR/NP	0	0	0	0

BID = twice daily; BLQ = below the lower limit of quantification (HIV-1 RNA <500 copies/mL); CCR5 = chemokine (C-C motif) Receptor 5; CXCR4 = chemokine (C-X-C motif) Receptor 4; HIV = human immunodeficiency virus; No = number; N = No. of subjects with a tropism assessment at Baseline and who had treatment failure due to insufficient clinical response or No. of subjects who discontinued for any reason and who had a tropism assessment at Baseline; n = No. of subjects with the indicated tropism result; NR/NP = non-reportable/non-phenotypable; QD = once daily; RNA = ribonucleic acid.

a. This table only includes subjects with a CCR5, dual/mixed, or NR/NP result at Baseline; no subject had CXCR4 or BLQ tropism result at Baseline.
b. This table only includes subjects with a CCR5, CXCR4, dual/mixed, or NR/NP result at time of treatment failure or discontinuation.
c. The assessment for time of treatment failure was defined as the last on treatment assessment. The No. of subjects in the table do not match N due to reasons as stated below:
d. One (1) subject (CCR5 tropism result at Baseline), 1 subject (dual/mixed tropism result at Baseline) and 1 subject (NR/NP tropism result at Baseline) all had BLQ tropism result at time of treatment failure.
e. Ten (10) subjects (CCR5 tropism result at Baseline), 1 subject (dual/mixed tropism result at Baseline) and 1 subject (NR/NP tropism result at Baseline) all had BLQ tropism result at time of treatment failure
f. Seven (7) subjects (CCR5 tropism at Baseline) had BLQ tropism results at time of treatment failure.
g. One hundred and thirty-five (135) subjects (CCR5 tropism result at Baseline), 2 subjects (dual/mixed tropism result at Baseline), and 2 subjects (NR/NP tropism result at Baseline) had BLQ tropism results at time of discontinuation. Eighteen (18) subjects (CCR5 tropism result at Baseline), 1 subject (dual/mixed tropism result at Baseline), and 1 subject (NR/NP tropism result at Baseline) had missing tropism results at time of discontinuation.
h. Fifty-five (55) subjects (CCR5 tropism result at Baseline), 1 subject (dual/mixed tropism result at Baseline), and 1 subject (NR/NP tropism result at Baseline) had BLQ tropism results at time of discontinuation. Seven (7) subjects (CCR5 tropism result at Baseline) and 1 subject (NR/NP tropism result at Baseline) had missing tropism results at time of discontinuation.
i. Eighty (80) subjects (CCR5 tropism result at Baseline), 1 subject (dual/mixed tropism result at Baseline), and 1 subject (NR/NP tropism result at Baseline) had BLQ tropism results at time of discontinuation. Eleven (11) subjects (CCR5 tropism result at Baseline) and 1 subject (dual/mixed tropism result at Baseline) had missing tropism results at time of discontinuation.

Table 35. Change in Tropism Result Between Baseline and Time of Treatment Failure or Discontinuation

Treatment Group	Tropism at Baseline[a]	Tropism at Time of Treatment Failure or Discontinuation[b]			
		CCR5 n	CXCR4 n	Dual/Mixed n	NR/NP n
Time of Treatment Failure[c]					
Maraviroc 300 mg QD → OL BID (All subjects) N=174 n=27[d, e]	CCR5	9	0	4	6
	Dual/mixed	0	0	5	0
Maraviroc 300 mg QD → OL BID (Subjects entering OL) N=130 n=16[d, f]	CCR5	4	0	4	4
	Dual/mixed	0	0	2	0
Time of Discontinuation					
Maraviroc 300 mg QD → OL BID (All subjects) N=174 n=77[g, h]	CCR5	25	0	5	9
	Dual/mixed	0	0	6	0
Maraviroc 300 mg QD → OL BID (Subjects entering OL) N=130 n=33[g, i]	CCR5	11	0	5	5
	Dual/mixed	0	0	2	0

BID = twice daily; CCR5 chemokine (C-C motif) Receptor 5; CXCR4 = chemokine (C-X-C motif) Receptor 4; OL = open-label; N = number of subjects with a tropism result at Baseline; NR/NP = non-reportable/non-phenotypable; QD = once daily.

a. Includes subjects with a CCR5 or dual/mixed result at Baseline.
b. Includes subjects with a CCR5, CXCR4, dual/mixed or NR/NP result at time of treatment failure or discontinuation.
c. The assessment for time of treatment failure was defined as the last on-treatment assessment.
d. n = number of subjects with a tropism result at Baseline and who had treatment failure due to insufficient clinical response.
e. The number of subjects in the table do not match n due to 1 subject with NR/NP at Baseline, and 2 subjects who had a CCR5 tropism result at Baseline with a viral load below the limit of quantification (<500 copies/mL) at time of treatment failure (tropism result either cancelled or censored).
f. The number of subjects in the table do not match n due to 1 subject with NR/NP, and 1 subject who had a CCR5 tropism result at Baseline with a viral load below the limit of quantification (<500 copies/mL) at time of treatment failure (tropism result either cancelled or censored).
g. n = number of subjects with a tropism result at Baseline who had discontinued study treatment.
h. The number of subjects in the table do not match n due to 2 subjects with NR/NP at Baseline, 27 subjects who had a CCR5 tropism result at Baseline with a viral load below the limit of quantification (<500 copies/mL) at time of discontinuation (tropism result either cancelled or censored), and 3 subjects with no tropism assessment at time of discontinuation.
i. The number of subjects in the table do not match n due to 1 subject with NR/NP at Baseline and 9 subjects who had a CCR5 tropism result at Baseline with a viral load below the limit of quantification (<500 copies/mL) at time of discontinuation (tropism result either cancelled or censored).

Safety Results: The number of subjects evaluable for safety included 174 in maraviroc 300 mg QD, 360 in maraviroc 300 mg BID and 361 in efavirenz, of which 151 subjects (86.8%) in maraviroc 300 mg QD, 319 subjects (88.6%) in maraviroc 300 mg BID and 327 subjects (90.6%) in efavirenz experienced non-serious AEs.

Table 36 summarizes the treatment-emergent and treatment-related AEs experienced by ≥5% of subjects in the double-blind/OL phase.

Table 37 summarizes the treatment-emergent non-serious AEs experienced by ≥5% of subjects in the double-blind phase.

Table 36. Percentage of Subjects Reporting Adverse Events – All Causality (Treatment-Related) Events Reported by ≥5% of Subjects in Either Treatment Group (Double-Blind/Open-Label Phase)

Percentage of Subjects All Causality (Treatment-Related)	Maraviroc 300 mg QD N=174	Maraviroc 300 mg OL BID N=130
Nausea	28.2% (24.1%)	6.9% (3.1%)
Headache	19.0% (14.4%)	7.7% (3.8%)
Fatigue	16.1% (12.1%)	4.6% (2.3%)
Diarrhoea	14.4% (7.5%)	7.7% (2.3%)
Dizziness	12.1% (9.8%)	1.5% (0.8%)
Abnormal dreams	11.5% (11.5%)	0.8% (0.8%)
Abdominal pain	10.9% (6.3%)	6.9% (5.4%)
Upper respiratory tract infection	9.8% (0.6%)	12.3% (0%)
Vomiting	9.8% (6.9%)	5.4% (0%)
Insomnia	8.6% (6.9%)	2.3% (2.3%)
Anaemia	7.5% (3.4%)	2.3% (0.8%)
Cough	6.9% (2.3%)	4.6% (0.8%)
Rash[a]	6.3% (4.0%)	3.8% (1.5%)
Abdominal distension	6.3% (4.0%)	1.5% (0.8%)
Anorexia	6.3% (4.6%)	1.5% (1.5%)
ALT increased	5.7% (4.6%)	3.1% (2.3%)
Asthenia	5.2% (4.0%)	4.6% (2.3%)
Pyrexia	5.2% (1.1%)	4.6% (1.5%)
AST increased	5.2% (4.0%)	3.1% (2.3%)
Depression	5.2% (3.4%)	3.1% (0%)
Constipation	5.2% (3.4%)	2.3% (1.5%)
Bronchitis	4.6% (0.6%)	9.2% (0%)
Nasopharyngitis	4.0% (0%)	10.0% (0%)
Arthralgia	3.4% (1.7%)	5.4% (0.8%)

Non SAE and SAE results are not separated out.
ALT = alanine aminotransferase; AST = aspartate aminotransferase; BID = twice a day; OL = open-label; QD = once a day; N = number of subjects in the treatment group in the indicated population; SAE = serious adverse event.

a. There were 9 reports of other types of all causality rash including pustular rash (1 subject in maraviroc 300 mg QD treatment group and 1 subject on open label maraviroc 300 mg BID), erythematous rash (1 subject in the maraviroc 300 mg QD treatment group), generalised rash (1 subject in the maraviroc 300 mg QD treatment group), macular rash (1 subject in the maraviroc 300 mg QD treatment group), papular rash (2 subjects in the maraviroc 300 mg QD treatment group and 1 subject on open label maraviroc 300 mg BID) and maculo-papular rash (1 subject on open label maraviroc 300 mg BID).

Table 37. Treatment-Emergent Non-Serious Adverse Events (All Causalities) at a Frequency Rate ≥5%

Adverse Event	Maraviroc 300 mg QD n (%)	Maraviroc 300 mg BID n (%)	Efavirenz n (%)
Number (%) of subjects:			
Evaluable for adverse events	174	360	361
With adverse events	151 (86.8)	319 (88.6)	327 (90.6)
System Organ Class and MedDRA Preferred Term			
Blood and lymphatic system disorders	12 (6.9)	27 (7.5)	18 (5.0)
Anaemia	12 (6.9)	27 (7.5)	18 (5.0)
Eye disorders	11 (6.3)	11 (3.1)	25 (6.9)
Conjunctivitis	11 (6.3)	11 (3.1)	25 (6.9)
Gastrointestinal disorders	108 (62.1)	230 (63.9)	235 (65.1)
Abdominal distension	12 (6.9)	21 (5.8)	20 (5.5)
Abdominal pain	30 (17.2)	53 (14.7)	53 (14.7)
Abdominal pain upper	7 (4.0)	22 (6.1)	23 (6.4)
Constipation	13 (7.5)	37 (10.3)	20 (5.5)
Diarrhoea	46 (26.4)	90 (25.0)	111 (30.7)
Dyspepsia	9 (5.2)	26 (7.2)	38 (10.5)
Flatulence	10 (5.7)	26 (7.2)	13 (3.6)
Gastritis	5 (2.9)	16 (4.4)	22 (6.1)
Haemorrhoids	6 (3.4)	25 (6.9)	16 (4.4)
Nausea	60 (34.5)	138 (38.3)	132 (36.6)
Vomiting	28 (16.1)	53 (14.7)	61 (16.9)
General disorders and administration site conditions	66 (37.9)	118 (32.8)	134 (37.1)
Asthenia	17 (9.8)	29 (8.1)	40 (11.1)
Chest pain	6 (3.4)	17 (4.7)	25 (6.9)
Fatigue	37 (21.3)	64 (17.8)	60 (16.6)
Influenza like illness	14 (8.0)	21 (5.8)	22 (6.1)
Pyrexia	16 (9.2)	21 (5.8)	30 (8.3)
Infections and infestations	89 (51.1)	219 (60.8)	201 (55.7)
Bronchitis	28 (16.1)	64 (17.8)	49 (13.6)
Gastroenteritis	10 (5.7)	27 (7.5)	33 (9.1)
Herpes zoster	4 (2.3)	18 (5.0)	16 (4.4)
Influenza	15 (8.6)	56 (15.6)	50 (13.9)
Nasopharyngitis	24 (13.8)	70 (19.4)	48 (13.3)
Pharyngitis	15 (8.6)	24 (6.7)	33 (9.1)
Sinusitis	4 (2.3)	29 (8.1)	28 (7.8)
Syphilis	10 (5.7)	16 (4.4)	13 (3.6)
Upper respiratory tract infection	32 (18.4)	82 (22.8)	78 (21.6)
Urinary tract infection	7 (4.0)	15 (4.2)	25 (6.9)
Investigations	15 (8.6)	22 (6.1)	14 (3.9)
Alanine aminotransferase increased	15 (8.6)	20 (5.6)	11 (3.0)
Aspartate aminotransferase increased	12 (6.9)	13 (3.6)	12 (3.3)
Metabolism and nutrition disorders	18 (10.3)	34 (9.4)	36 (10.0)
Decreased appetite	18 (10.3)	34 (9.4)	36 (10.0)
Musculoskeletal and connective tissue disorders	46 (26.4)	107 (29.7)	111 (30.7)
Arthralgia	17 (9.8)	37 (10.3)	30 (8.3)
Back pain	18 (10.3)	44 (12.2)	44 (12.2)
Muscle spasms	9 (5.2)	16 (4.4)	22 (6.1)
Myalgia	14 (8.0)	29 (8.1)	28 (7.8)
Pain in extremity	15 (8.6)	27 (7.5)	23 (6.4)
Neoplasms benign, malignant and unspecified (incl cysts and polyps	10 (5.7)	6 (1.7)	14 (3.9)
Skin papilloma	10 (5.7)	6 (1.7)	14 (3.9)
Nervous system disorders	71 (40.8)	163 (45.3)	185 (51.2)
Dizziness	25 (14.4)	62 (17.2)	116 (32.1)
Dysgeusia	10 (5.7)	10 (2.8)	11 (3.0)

Table 37. Treatment-Emergent Non-Serious Adverse Events (All Causalities) at a Frequency Rate ≥5%

Adverse Event	Maraviroc 300 mg QD n (%)	Maraviroc 300 mg BID n (%)	Efavirenz n (%)
Headache	44 (25.3)	109 (30.3)	105 (29.1)
Paraesthesia	7 (4.0)	19 (5.3)	13 (3.6)
Somnolence	6 (3.4)	18 (5.0)	13 (3.6)
Psychiatric disorders	56 (32.2)	102 (28.3)	111 (30.7)
Abnormal dreams	20 (11.5)	22 (6.1)	46 (12.7)
Anxiety	8 (4.6)	21 (5.8)	26 (7.2)
Depression	18 (10.3)	40 (11.1)	28 (7.8)
Insomnia	20 (11.5)	48 (13.3)	44 (12.2)
Sleep disorder	7 (4.0)	12 (3.3)	19 (5.3)
Respiratory, thoracic and mediastinal disorders	31 (17.8)	73 (20.3)	79 (21.9)
Cough	22 (12.6)	51 (14.2)	66 (18.3)
Oropharyngeal pain	9 (5.2)	30 (8.3)	21 (5.8)
Skin and subcutaneous tissue disorders	42 (24.1)	65 (18.1)	110 (30.5)
Eczema	6 (3.4)	9 (2.5)	22 (6.1)
Lipodystrophy acquired	7 (4.0)	12 (3.3)	21 (5.8)
Pruritus	9 (5.2)	8 (2.2)	26 (7.2)
Rash	25 (14.4)	38 (10.6)	56 (15.5)
Vascular disorders	6 (3.4)	25 (6.9)	23 (6.4)
Hypertension	6 (3.4)	25 (6.9)	23 (6.4)

Subjects are only counted once per treatment for each row.
Includes data up to 7 days after last dose of study drug.
MedDRA (v14.0) coding dictionary applied.
BID = twice daily; incl = including; MedDRA = medical dictionary for regulatory activities; n = number of subjects; QD = once daily; v = version.

The treatment-emergent treatment-related non-serious AEs in the double-blind phase are summarized in Table 38.

Table 38. Percentage of Subjects Reporting Treatment-Emergent Adverse Events - All Causality (Treatment-Related): Events Reported by ≥5% of Subjects in Any Treatment Group

Percentage of Subjects All-Causality (Treatment-Related) MedDRA Preferred Term	Maraviroc 300 mg BID (N=360) %	Efavirenz 600 mg QD (N=361) %
Nausea	36.1 (30.6)	34.6 (27.7)
Headache	25.3 (18.3)	25.2 (16.6)
Diarrhoea	20.0 (8.1)	25.8 (12.7)
Fatigue	16.1 (10.3)	14.1 (8.9)
Dizziness	15.6 (11.4)	31.0 (27.7)
Upper respiratory tract infection	15.0 (0)	15.8 (0.3)
Vomiting	13.6 (7.5)	15.5 (10.2)
Nasopharyngitis	13.3 (0.3)	9.1 (0)
Bronchitis	13.1 (0)	9.4 (0.3)
Cough	11.4 (1.4)	13.0 (1.9)
Abdominal pain	11.4 (6.9)	11.9 (7.8)
Insomnia	10.3 (5.6)	9.7 (6.6)
Influenza	9.4 (0)	9.1 (0)
Constipation	7.8 (4.2)	3.6 (1.7)
Anaemia	7.8 (3.1)	5.0 (1.9)
Back pain	7.8 (1.4)	8.6 (2.5)
Asthenia	7.5 (6.4)	10.5 (8.0)
Rash[a]	7.2 (2.8)	13.6 (8.9)
Flatulence	6.7 (5.3)	3.0 (2.8)
Depression	6.7 (2.8)	5.5 (1.4)
Abnormal dreams	5.8 (5.8)	12.2 (11.9)
Pharyngolaryngeal pain	5.8 (1.1)	3.9 (0.3)
Arthralgia	5.8 (0.8)	4.7 (0.6)
Pyrexia	5.8 (0.3)	6.6 (1.9)
Anorexia	5.6 (3.9)	6.4 (3.9)
Dyspepsia	5.6 (3.6)	7.2 (5.3)
Myalgia	5.3 (1.9)	5.5 (1.7)
Abdominal pain upper	3.6 (1.7)	5.0 (3.9)
Sinusitis	3.3 (0)	5.3 (0)
Anxiety	3.1 (1.1)	5.0 (2.8)
Eczema	2.2 (0.3)	5.5 (1.4)
Conjunctivitis	2.2 (0)	5.0 (0.6)
Pruritus	1.9 (1.4)	6.1 (3.0)

Non SAE and SAE results are not separated out in the table.
BID = twice a daily; MedDRA = Medical Dictionary for Regulatory Activities; N = number of subjects in the treatment group in the indicated population; QD = once daily; SAEs = serious adverse events; TEAE = treatment-emergent adverse events.

a. Other types of all causality TEAEs of rash were reported for a number of subjects in each treatment group: rash erythematous (2 [0.6%] subjects in the maraviroc 300 mg BID treatment group and 1 [0.3%] subject in the efavirenz 600 mg QD treatment group), rash generalized (1 [0.3%] subject in the maraviroc 300 mg BID treatment group and 3 [0.8%] subjects in the efavirenz 600 mg QD treatment group), rash macular (5 [1.4%] subjects in each treatment group), rash maculo-papular (3 [0.8%] subjects in the maraviroc 300 mg BID treatment group and 5 [1.4%] subjects in the efavirenz 600 mg QD treatment group), rash papular (3 [0.8%] subjects in the maraviroc 300 mg BID treatment group and 5 [1.4%] subjects in the efavirenz 600 mg QD treatment group), and rash pruritic (3 [0.8%] subjects in the maraviroc 300 mg BID treatment group and 4 [1.1%] subjects in the efavirenz 600 mg QD treatment group).

A total of 22 subjects (12.6%) receiving maraviroc 300 mg QD and 17 subjects (13.1%) receiving OL maraviroc 300 mg BID reported treatment-emergent serious adverse events (SAEs) in the OL phase (Table 39). The SAEs were considered related to maraviroc by the Investigator for 4 subjects (2.3%) receiving maraviroc 300 mg QD and 4 subjects (3.1%) receiving OL maraviroc 300 mg BID as shown in Table 40.

Table 39. Serious Adverse Events

Subject Serial Number	Suspect Drug(s)	MedDRA Preferred Term (Reported Term)	Sponsor/Investigator Causality	Outcome
1	Maraviroc	Uterine leiomyoma (fibroids)	No/other illness	Recovered
2	Maraviroc	Urinary tract infection (urinary tract infection)	No/other	Recovered
3	Maraviroc	Localised infection (infected thumb)	No/other	Recovered
	Zidovudine W/Lamivudine	Localised infection (infected thumb)	No/other	
4	Maraviroc	Anaemia (anemia aggravated)	No/concomitant treatment/therapy	Recovered
	Zidovudine W/Lamivudine	Anaemia (anemia aggravated)	Yes/study drug	
5	Maraviroc	Suicidal ideation (suicidal ideation)	No/other illness	Recovered
	Zidovudine W/Lamivudine	Suicidal ideation (suicidal ideation)	No/other illness	
6	Maraviroc	Orchitis (epididymo-orchitis)	No/other illness	Recovered
	Zidovudine W/Lamivudine	Orchitis (epididymo-orchitis)	No/other illness	
7	Maraviroc	Myopericarditis (myopericarditis)	No/other illness	Recovered
8	Maraviroc	Cellulitis (cellulitis)	No/other	Recovered
	Zidovudine W/Lamivudine	Cellulitis (cellulitis)	No/other	
9	Maraviroc	Depression (depression)	No/other	Recovered
10	Maraviroc	Pleural effusion (pleural effusion)	No/other	Recovered
	Nelfinavir	Pleural effusion (pleural effusion)	No/other	
	Zidovudine W/Lamivudine	Pleural effusion (pleural effusion)	No/other	
11	Maraviroc	Rash (rash)	Yes/study drug	Recovered with sequelae
		Hepatitis toxic (toxic hepatitis)	Yes/study drug	
	Zidovudine W/Lamivudine	Rash (rash)	Yes/study drug	
		Hepatitis toxic (toxic hepatitis)	Yes/study drug	
12	Maraviroc	Stevens-Johnson syndrome (stevens-johnson syndrome)	Yes/study drug	Recovered
	Dapsone		Yes/concomitant treatment/therapy	
	Zidovudine W/Lamivudine	Stevens-Johnson syndrome (stevens-johnson syndrome)	No/other	
		Stevens-Johnson syndrome (stevens-johnson syndrome)		
13	Maraviroc	Hypersensitivity (hypersensitivity reaction)	No/other	Recovered
	Blinded therapy	Hypersensitivity (hypersensitivity reaction)	No/other	

Table 39. Serious Adverse Events

Subject Serial Number	Suspect Drug(s)	MedDRA Preferred Term (Reported Term)	Sponsor/Investigator Causality	Outcome
14	Maraviroc	Tinnitus (tinnitus)	No/other	Recovered
		Dyspraxia (dyspraxia)	No/other	
		Vertigo (vertigo)	No/other	
		Tinnitus (tinnitus)		
	Zidovudine	Dyspraxia (dyspraxia)	No/other	
	W/Lamivudine	Vertigo (vertigo)	No/other	
			No/other	
15	Maraviroc	Suicide attempt (suicide attempt)	No/other	Recovered
	Zidovudine	Suicide attempt (suicide attempt)	No/other	
	W/Lamivudine			
16	Maraviroc	Neutropenia (neutropenia)	No/other	Recovered
	Blinded therapy	Neutropenia (neutropenia)	No/other	
	Zidovudine	Neutropenia (neutropenia)	Yes/study drug	
	W/Lamivudine			
17	Maraviroc	Hypersensitivity (hypersensitivity reaction)	No/other	Recovered
	Abacavir/Lamivudine	Hypersensitivity (hypersensitivity reaction)	Yes/study drug	
	Efavirenz	Hypersensitivity (hypersensitivity reaction)	No/other	
18	Maraviroc	Pyrexia (fever)	No/other	Recovered
		Diarrhoea (diarrhoea)	No/other	
	Blinded therapy	Pyrexia (fever)	No/other illness	
	Zidovudine	Diarrhoea (diarrhoea)	No/other illness	
	W/Lamivudine	Pyrexia (fever)	No/other	
		Diarrhoea (diarrhoea)	No/other	
19	Maraviroc	Suicide attempt (suicide attempt)	No/other illness	Recovered with sequelae
	Zidovudine	Suicide attempt (suicide attempt)	No/other illness	
	W/Lamivudine			
20	Maraviroc	Duodenal ulcer (duodenal ulcer)	No/concomitant treatment/therapy	Recovered
	Blinded therapy	Duodenal ulcer (duodenal ulcer)	No/concomitant treatment/therapy	
21	Maraviroc	Pneumocystis jiroveci pneumonia (pneumocystis carinii pneumonia)	No/other illness	Recovered
	Zidovudine	Pneumocystis jiroveci pneumonia (pneumocystis	No/other illness	
	W/Lamivudine	carinii pneumonia)		

Table 39. Serious Adverse Events

Subject Serial Number	Suspect Drug(s)	MedDRA Preferred Term (Reported Term)	Sponsor/Investigator Causality	Outcome
22	Maraviroc	Haemorrhoids (haemorrhoids)	No/other illness	Not recovered
		Rectal polyp (rectal polyp)	No/other illness	
	Zidovudine W/Lamivudine	Haemorrhoids (haemorrhoids)	No/other illness	
		Rectal polyp (rectal polyp)	No/other illness	
23	Maraviroc	Pyrexia (fever)	No/other illness	Not recovered
		Malaise (malaise)	No/other illness	
24	Maraviroc	Haemoptysis (hemoptysis)	No/other illness	Not recovered
		Bronchitis (acute bronchitis)	No/other illness	
		Small cell lung cancer stage unspecified (small cell lung cancer)	No/other illness	
	Zidovudine W/Lamivudine	Haemoptysis (hemoptysis)	No/other illness	
		Bronchitis (acute bronchitis)	No/other illness	
		Small cell lung cancer stage unspecified (small cell lung cancer)	No/other illness	
25	Maraviroc	Aspartate aminotransferase increased (SGOT increased)	No/other illness	Recovered
26	Maraviroc	Nephrolithiasis (renal stone)	No/other illness	Recovered
	Zidovudine W/Lamivudine	Nephrolithiasis (renal stone)	No/other illness	
27	Maraviroc	Fracture (fracture)	No/other illness	Recovered
		Haematotympanum (hemotympanum)	No/other illness	
28	Blinded therapy	Chest pain (chest pain)	No/other	Recovered
29	Blinded therapy	Mental status changes (mental status changes)	No/concomitant treatment/therapy	Recovered
		Rhabdomyolysis (rhabdomyolysis)	No/other	
	Zidovudine W/Lamivudine	Mental status changes (mental status changes)	No/concomitant treatment/therapy	
		Rhabdomyolysis (rhabdomyolysis)	No/other	

Table 39. Serious Adverse Events

Subject Serial Number	Suspect Drug(s)	MedDRA Preferred Term (Reported Term)	Sponsor/Investigator Causality	Outcome
30	Blinded therapy	Rash erythematous (erythematous rash)	Yes/study drug	Recovered
		Myalgia (myalgias)	Yes/study drug	
		Arthralgia (arthralgia)	Yes/study drug	
		Asthenia (weakness)	Yes/study drug	
		Pyrexia (fever)	No/other	
		Anorexia (loss of appetite)	No/other	
		Rash morbilliform (morbilliform rash)	No/other	
	Emcitricitabine/ tenofavir disoproxil fumarate	Rash erythematous (erythematous rash)	Yes/study drug	
		Myalgia (myalgias)	Yes/study drug	
		Arthralgia (arthralgia)	Yes/study drug	
		Asthenia (weakness)	Yes/study drug	
		Pyrexia (fever)	No/other	
		Anorexia (loss of appetite)	No/other	
		Rash morbilliform (morbilliform rash)	No/other	
	Zidovudine W/Lamivudine	Rash erythematous (erythematous rash)	No/other	
		Myalgia (myalgias)	No/other	
		Arthralgia (arthralgia)	No/other	
		Asthenia (weakness)	No/other	
		Pyrexia (fever)	No/other	
		Anorexia (loss of appetite)	No/other	
		Rash morbilliform (morbilliform rash)	No/other	
31	Blinded therapy	Thrombophlebitis (thrombophlebitis leg)	No/other	Recovered
32	Blinded therapy	Calculus ureteric (ureteric calculus)	No/other	Recovered
33	Blinded therapy	Hyperventilation (hyperventilation)	No/other	Recovered
34	Blinded therapy	Anaemia (anemia)	Yes/study drug	Recovered
		Leukopenia (leucopenia)	Yes/study drug	
	Zidovudine W/Lamivudine	Anaemia (anemia)	Yes/study drug	
		Leukopenia (leucopenia)	Yes/study drug	
35	Blinded therapy	Alanine aminotransferase increased (ALT increased)	No/concomitant treatment/therapy	Recovered
	Zidovudine W/Lamivudine		No/concomitant treatment/therapy	
		Alanine aminotransferase increased (ALT increased)		
36	Blinded therapy	Anaemia (anemia)	No/concomitant treatment/therapy	Recovered
	Zidovudine W/Lamivudine	Anaemia (anemia)	Yes/study drug	

Table 39. Serious Adverse Events

Subject Serial Number	Suspect Drug(s)	MedDRA Preferred Term (Reported Term)	Sponsor/Investigator Causality	Outcome
37	Blinded therapy	Non-Hodgkin's lymphoma (non-hodgkin's lymphoma)	No/disease under study(protocol indication)	Death
	Zidovudine W/Lamivudine	Non-Hodgkin's lymphoma (non-hodgkin's lymphoma)	No/disease under study(protocol indication)	
38	Blinded therapy	Disseminated tuberculosis (miliary tuberculosis)	No/other illness	Recovering
39	Blinded therapy	Completed suicide (suicide)	No/other	Death
40	Blinded therapy	Pyrexia (fever)	No/disease under study(protocol indication)	Recovered
		Headache (headache)	No/disease under study(protocol indication)	
41	Blinded therapy	Anaemia (anemia)	No/concomitant treatment/therapy	Recovered
	Zidovudine W/Lamivudine	Anaemia (anemia)	Yes/study drug	
42	Blinded therapy	Uterine cervical laceration (cervical laceration)	No/other illness	Recovered
43	Blinded therapy	Anogenital warts (condyloma anal)	No/other illness	Recovered
	Zidovudine W/Lamivudine	Anogenital warts (condyloma anal)	No/other	
44	Blinded therapy	Anaemia (anemia)	No/concomitant treatment/therapy	Recovered
	Zidovudine W/Lamivudine	Anaemia (anemia)	Yes/study drug	
45	Blinded therapy	Pyrexia (febrile illness)	No/disease under study(protocol indication)	Not recovered
		Kaposi's sarcoma (kaposi's sarcoma)	No/disease under study(protocol indication)	
	Zidovudine W/Lamivudine	Pyrexia (febrile illness)	No/disease under study(protocol indication)	
		Kaposi's sarcoma (kaposi's sarcoma)	No/disease under study(protocol indication)	
46	Blinded therapy	Bronchopneumonia (bronchopneumonia)	No/other illness	Recovered
	Zidovudine W/Lamivudine	Bronchopneumonia (bronchopneumonia)	No/other illness	
47	Blinded therapy	Ankle fracture (malleolar fracture)	No/other	Recovered
	Zidovudine W/Lamivudine	Ankle fracture (malleolar fracture)	No/other	

Table 39. Serious Adverse Events

Subject Serial Number	Suspect Drug(s)	MedDRA Preferred Term (Reported Term)	Sponsor/Investigator Causality	Outcome

ALT = alanine transaminase; SGOT = serum glutaminic-oxaloacetic transaminase.

Table 40. Treatment-Emergent Treatment-Related Serious Adverse Events (Events Related to Maraviroc)

Subject Serial Number	Serious Adverse Event(s)	Outcome
Maraviroc 300 mg QD		
1	Rash erythematous[a] Myalgia[a] Arthralgia[a] Asthenia[a]	Recovered
2	Hepatitis toxic[a] Rash[a]	Recovered with sequelae
3	Stevens-Johnson syndrome[a]	Recovered
4	Anaemia[b] Leucopenia[b]	Recovered
Maraviroc 300 mg OL BID		
5	Transient ischaemic attack	Recovered
6	Multiple myeloma	Recovering
7	Blood creatine phosphokinase increased	Recovered
8	Gamma-glutamyltransferase increased	Recovered

BID = twice daily, OL = open-label; QD = once daily.
a. Subject permanently discontinued due to this adverse event.
b. Subject temporarily discontinued due to this adverse event.

Forty-seven (47) subjects (27.0%) in maraviroc 300 mg QD, 77 subjects (21.4%) in maraviroc 300 mg BID and 82 subjects (22.7%) in efavirenz experienced SAEs as summarized in Table 41

Table 41. Treatment-Emergent Serious Adverse Events (All-Causalities)

Adverse Event System Organ Class/Preferred term	Maraviroc 300 mg QD n (%)	Maraviroc 300 mg BID n (%)	Efavirenz 600 mg QD n (%)
Number (%) of subjects:			
Evaluable for adverse events	174	360	361
With adverse events	47 (27.0)	77 (21.4)	82 (22.7)
Blood and lymphatic system disorders	8 (4.6)	9 (2.5)	10 (2.8)
Anaemia	6 (3.4)	7 (1.9)	6 (1.7)
Leukocytosis	0	0	1 (0.3)
Neutropenia	3 (1.7)	2 (0.6)	2 (0.6)
Pancytopenia	0	0	2 (0.6)
Cardiac disorders	2 (1.1)	5 (1.4)	5 (1.4)
Acute myocardial infarction	0	1 (0.3)	2 (0.6)
Angina unstable	1 (0.6)	1 (0.3)	1 (0.3)
Cardiopulmonary failure	0	0	1 (0.3)
Myocardial infarction	0	2 (0.6)	1 (0.3)
Pericardial effusion	1 (0.6)	0	0
Pulseless electrical activity	0	1 (0.3)	0
Congenital, familial and genetic disorders	0	0	1 (0.3)
Bicuspid aortic valve	0	0	1 (0.3)
Ear and labyrinth disorders	2 (1.1)	0	0
Haematotympanum	1 (0.6)	0	0
Tinnitus	1 (0.6)	0	0
Vertigo	1 (0.6)	0	0
Eye disorders	0	1 (0.3)	0
Diabetic eye disease	0	1 (0.3)	0
Uveitis	0	1 (0.3)	0
Gastrointestinal disorders	8 (4.6)	12 (3.3)	10 (2.8)
Abdominal pain	1 (0.6)	4 (1.1)	1 (0.3)
Abdominal pain lower	1 (0.6)	0	0
Anal fistula	0	1 (0.3)	2 (0.6)
Ascites	1 (0.6)	0	0
Colitis	0	0	1 (0.3)
Diarrhoea	2 (1.1)	2 (0.6)	0
Duodenal ulcer	1 (0.6)	0	0
Gastric ulcer	0	0	1 (0.3)
Gastritis	0	1 (0.3)	1 (0.3)
Gastrointestinal haemorrhage	1 (0.6)	0	0
Haemorrhoids	1 (0.6)	1 (0.3)	0
Ileus	0	0	1 (0.3)
Inguinal hernia	0	0	1 (0.3)
Mesenteric vein thrombosis	0	0	1 (0.3)
Nausea	0	1 (0.3)	0
Pancreatitis	0	1 (0.3)	1 (0.3)
Rectal haemorrhage	0	0	1 (0.3)
Rectal polyp	1 (0.6)	0	0
Small intestinal obstruction	0	1 (0.3)	0
Vomiting	0	2 (0.6)	0
General disorders and administration site conditions	6 (3.4)	4 (1.1)	7 (1.9)
Asthenia	1 (0.6)	0	0
Chest pain	2 (1.1)	0	0
Influenza like illness	0	0	2 (0.6)
Pyrexia	4 (2.3)	4 (1.1)	5 (1.4)
Sudden cardiac death	0	0	1 (0.3)
Hepatobiliary disorders	1 (0.6)	3 (0.8)	3 (0.8)
Biliary colic	0	0	1 (0.3)
Cholelithiasis	0	2 (0.6)	2 (0.6)
Hepatitis	0	0	1 (0.3)
Hepatitis toxic	1 (0.6)	0	0

Table 41. Treatment-Emergent Serious Adverse Events (All-Causalities)

Adverse Event System Organ Class/Preferred term	Maraviroc 300 mg QD n (%)	Maraviroc 300 mg BID n (%)	Efavirenz 600 mg QD n (%)
Hypertransaminasaemia	0	1 (0.3)	0
Immune system disorders	1 (0.6)	1 (0.3)	1 (0.3)
Anaphylactic shock	1 (0.6)	0	0
Drug hypersensitivity	0	1 (0.3)	0
Hypersensitivity	0	0	1 (0.3)
Infections and infestations	9 (5.2)	24 (6.7)	25 (6.9)
Anal abscess	0	0	1 (0.3)
Anal fistula infection	0	1 (0.3)	0
Anogenital warts	1 (0.6)	1 (0.3)	0
Appendicitis	0	3 (0.8)	3 (0.8)
Appendicitis perforated	0	0	1 (0.3)
Bronchitis	1 (0.6)	0	2 (0.6)
Bronchopneumonia	1 (0.6)	1 (0.3)	1 (0.3)
Cellulitis	0	1 (0.3)	1 (0.3)
Cryptosporidiosis infection	1 (0.6)	0	0
Disseminated tuberculosis	1 (0.6)	0	0
Diverticulitis	0	0	1 (0.3)
Hepatitis A	0	1 (0.3)	0
Hepatitis C	0	1 (0.3)	0
Herpes zoster	0	0	1 (0.3)
Intervertebral discitis	1 (0.6)	0	0
Lobar pneumonia	0	2 (0.6)	2 (0.6)
Localised infection	1 (0.6)	0	0
Lower respiratory tract infection	0	1 (0.3)	1 (0.3)
Meningitis	0	1 (0.3)	0
Meningitis bacterial	0	1 (0.3)	0
Neurosyphilis	0	1 (0.3)	1 (0.3)
Orchitis	1 (0.6)	0	0
Osteomyelitis	0	0	1 (0.3)
Parasitic gastroenteritis	1 (0.6)	0	0
Pelvic inflammatory disease	0	0	1 (0.3)
Penile infection	0	1 (0.3)	0
Peritoneal abscess	0	0	1 (0.3)
Pneumocystis jiroveci infection	1 (0.6)	0	0
Pneumocystis jiroveci pneumonia	1 (0.6)	1 (0.3)	0
Pneumonia	1 (0.6)	3 (0.8)	5 (1.4)
Pneumonia staphylococcal	0	0	1 (0.3)
Pulmonary tuberculosis	0	2 (0.6)	3 (0.8)
Sepsis	0	0	1 (0.3)
Sinobronchitis	0	1 (0.3)	0
Sinusitis	0	1 (0.3)	0
Staphylococcal bacteraemia	1 (0.6)	0	0
Staphylococcal infection	1 (0.6)	0	0
Subcutaneous abscess	0	0	2 (0.6)
Syphilis	0	2 (0.6)	0
Upper respiratory tract infection	0	0	1 (0.3)
Urinary tract infection	0	0	1 (0.3)
Injury, poisoning and procedural complications	4 (2.3)	8 (2.2)	8 (2.2)
Ankle fracture	1 (0.6)	1 (0.3)	1 (0.3)
Chest injury	0	0	1 (0.3)
Concussion	0	0	1 (0.3)
Femoral neck fracture	0	1 (0.3)	0
Head injury	0	2 (0.6)	0
Heart injury	0	0	1 (0.3)
Hip fracture	0	1 (0.3)	0
Human bite	0	0	1 (0.3)

Table 41. Treatment-Emergent Serious Adverse Events (All-Causalities)

Adverse Event System Organ Class/Preferred term	Maraviroc 300 mg QD n (%)	Maraviroc 300 mg BID n (%)	Efavirenz 600 mg QD n (%)
Injury	0	1 (0.3)	0
Jaw fracture	2 (1.1)	0	0
Laceration	0	0	2 (0.6)
Limb injury	0	1 (0.3)	0
Multiple fractures	0	1 (0.3)	1 (0.3)
Overdose	0	0	2 (0.6)
Pubis fracture	0	1 (0.3)	0
Rib fracture	1 (0.6)	0	0
Skull fracture	1 (0.6)	0	0
Soft tissue injury	0	0	1 (0.3)
Spinal compression fracture	0	1 (0.3)	0
Tendon rupture	0	1 (0.3)	0
Whiplash injury	0	0	1 (0.3)
Investigations	4 (2.3)	5 (1.4)	9 (2.5)
Alanine aminotransferase increased	1 (0.6)	1 (0.3)	1 (0.3)
Aspartate aminotransferase increased	0	1 (0.3)	2 (0.6)
Blood creatine phosphokinase increased	1 (0.6)	2 (0.6)	3 (0.8)
Blood lactate dehydrogenase increased	0	0	1 (0.3)
Blood sodium decreased	0	0	1 (0.3)
Gamma-glutamyltransferase increased	1 (0.6)	0	2 (0.6)
Haemoglobin decreased	0	1 (0.3)	0
Hepatic enzyme increased	1 (0.6)	0	1 (0.3)
Transaminases increased	0	1 (0.3)	1 (0.3)
Metabolism and nutrition disorders	1 (0.6)	2 (0.6)	1 (0.3)
Decreased appetite	1 (0.6)	1 (0.3)	0
Dehydration	0	0	1 (0.3)
Hyperkalaemia	0	1 (0.3)	0
Musculoskeletal and connective tissue disorders	2 (1.1)	3 (0.8)	1 (0.3)
Arthralgia	1 (0.6)	0	0
Back pain	0	2 (0.6)	0
Flank pain	0	0	1 (0.3)
Myalgia	1 (0.6)	0	0
Osteoarthritis	0	1 (0.3)	0
Pain in extremity	0	1 (0.3)	0
Rhabdomyolysis	1 (0.6)	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	6 (3.4)	7 (1.9)	10 (2.8)
Basal cell carcinoma	0	0	1 (0.3)
Breast cancer in situ	1 (0.6)	0	0
Castleman's disease	0	0	1 (0.3)
Diffuse large B-cell lymphoma	0	1 (0.3)	0
Fibroma	1 (0.6)	0	0
Hodgkin's disease	0	2 (0.6)	3 (0.8)
Kaposi's sarcoma	1 (0.6)	0	0
Metastases to bone	0	1 (0.3)	0
Metastatic neoplasm	0	0	1 (0.3)
Multiple myeloma	1 (0.6)	0	0
Nasopharyngeal cancer	0	1 (0.3)	0
Neoplasm	0	1 (0.3)	0
Non-Hodgkin's lymphoma	1 (0.6)	0	1 (0.3)
Non-small cell lung cancer	0	0	1 (0.3)
Rectal cancer	0	0	1 (0.3)
Squamous cell carcinoma	1 (0.6)	0	0

Table 41. Treatment-Emergent Serious Adverse Events (All-Causalities)

Adverse Event System Organ Class/Preferred term	Maraviroc 300 mg QD n (%)	Maraviroc 300 mg BID n (%)	Efavirenz 600 mg QD n (%)
Thyroid cancer	0	1 (0.3)	0
Thyroid neoplasm	0	1 (0.3)	0
Vulval neoplasm	0	0	1 (0.3)
Nervous system disorders	5 (2.9)	8 (2.2)	6 (1.7)
Ataxia	0	0	2 (0.6)
Balance disorder	0	0	1 (0.3)
Cerebrovascular accident	0	1 (0.3)	0
Convulsion	1 (0.6)	1 (0.3)	2 (0.6)
Cranial nerve paralysis	0	0	1 (0.3)
Dysarthria	0	1 (0.3)	1 (0.3)
Dyspraxia	1 (0.6)	0	0
Encephalitis	1 (0.6)	0	0
Grand mal convulsion	0	0	1 (0.3)
Headache	1 (0.6)	1 (0.3)	1 (0.3)
Ischaemic stroke	0	1 (0.3)	0
Loss of consciousness	0	2 (0.6)	0
Monoparesis	0	1 (0.3)	0
Syncope	1 (0.6)	1 (0.3)	0
Thoracic outlet syndrome	0	1 (0.3)	0
Transient ischaemic attack	1 (0.6)	0	0
Vascular dementia	0	1 (0.3)	0
Pregnancy, puerperium and perinatal conditions	3 (1.7)	5 (1.4)	9 (2.5)
Abortion	0	0	1 (0.3)
Abortion spontaneous	0	0	1 (0.3)
Pregnancy	3 (1.7)	5 (1.4)	8 (2.2)
Psychiatric disorders	8 (4.6)	6 (1.7)	3 (0.8)
Completed suicide	1 (0.6)	0	0
Depression	1 (0.6)	2 (0.6)	0
Depression suicidal	1 (0.6)	0	0
Drug abuse	0	1 (0.3)	0
Drug dependence	1 (0.6)	0	0
Intentional self-injury	0	1 (0.3)	1 (0.3)
Major depression	0	1 (0.3)	0
Mental status changes	1 (0.6)	0	0
Post-traumatic stress disorder	0	1 (0.3)	0
Suicidal ideation	1 (0.6)	0	0
Suicide attempt	2 (1.1)	0	2 (0.6)
Renal and urinary disorders	2 (1.1)	0	4 (1.1)
Calculus bladder	0	0	1 (0.3)
Haematuria	0	0	1 (0.3)
Nephrolithiasis	1 (0.6)	0	0
Renal failure	0	0	1 (0.3)
Renal failure acute	1 (0.6)	0	1 (0.3)
Reproductive system and breast disorders	1 (0.6)	1 (0.3)	1 (0.3)
Cervix haemorrhage uterine	1 (0.6)	0	0
Epididymitis	0	1 (0.3)	0
Ovarian cyst	0	0	1 (0.3)
Testicular pain	0	1 (0.3)	0
Uterine cervical laceration	1 (0.6)	0	0
Respiratory, thoracic and mediastinal disorders	3 (1.7)	3 (0.8)	1 (0.3)
Atelectasis	1 (0.6)	0	0
Haemoptysis	1 (0.6)	0	0
Pleural effusion	1 (0.6)	0	0
Pneumothorax	0	0	1 (0.3)
Pulmonary embolism	1 (0.6)	3 (0.8)	0

Table 41. Treatment-Emergent Serious Adverse Events (All-Causalities)

Adverse Event System Organ Class/Preferred term	Maraviroc 300 mg QD n (%)	Maraviroc 300 mg BID n (%)	Efavirenz 600 mg QD n (%)
Skin and subcutaneous tissue disorders	3 (1.7)	2 (0.6)	3 (0.8)
Dermal cyst	0	0	1 (0.3)
Drug eruption	0	1 (0.3)	0
Penile ulceration	0	1 (0.3)	0
Rash	1 (0.6)	0	1 (0.3)
Rash erythematous	1 (0.6)	0	0
Rash pruritic	0	0	1 (0.3)
Stevens-Johnson syndrome	1 (0.6)	0	0
Social circumstances	1 (0.6)	1 (0.3)	0
Drug abuser	1 (0.6)	0	0
Pregnancy of partner	0	1 (0.3)	0
Surgical and medical procedures	0	2 (0.6)	0
Cholecystectomy	0	1 (0.3)	0
Finger amputation	0	1 (0.3)	0
Vascular disorders	1 (0.6)	1 (0.3)	1 (0.3)
Deep vein thrombosis	0	1 (0.3)	1 (0.3)
Hypertension	1 (0.6)	0	0

Subjects were counted once per treatment for each row.
MedDRA (v14.0) coding dictionary applied.
BID = twice daily; incl = including; MedDRA = medical dictionary for regulatory activities; n = number of subjects; QD = once daily.

Treatment-related SAEs for maraviroc 300 mg BID and efavirenz 600 mg QD are summarized in Table 42 and Table 43 respectively.

Table 42. Treatment-Emergent Treatment-Related Serious Adverse Events (Events Related to Maraviroc 300 mg BID)

Subject Serial Number	SAE(s)	Outcome[a]
1	Deep vein thrombosis	Not recovered
	Nasopharyngeal cancer[b]	Death
2	Vomiting[c]	Recovered
	Nausea[c]	
3	Transaminases increased[c]	Recovered
	Anorexia[c]	
	Abdominal pain[c]	
4	Blood creatine phosphokinase increased	Recovered
5	Neutropenia[d]	Recovered
6	Hodgkin's disease[c]	Not recovered
	Anaemia	
7	Syncope[c]	Recovered
8	Diffuse large B-cell lymphoma[b, c]	Death
9	Depression[c]	Recovered
10	Transaminases increased[c]	Recovering

BID = twice daily; SAE = serious adverse event.
a. Subject outcome rather than SAE outcome.
b. Subject died due to this SAE.
c. Subject permanently discontinued due to this SAE.
d. Subject temporarily discontinued due to this SAE.

Table 43. Treatment-Emergent Treatment-Related Serious Adverse Events (Events Related to Efavirenz 600 mg QD)

Subject Serial Number	SAEs	Outcome[a]
1	Pancytopenia[b]	Not recovered
2	Anaemia[b]	Recovered
3	Anaemia[b]	Recovered
4	Haematuria[c]	Recovered
	Flank pain[c]	
5	Myocardial infarction[b]	Recovered
6	Rash macular[b]	Recovered
	Hepatic enzyme increased[b]	
7	Rash[b]	Recovered
8	GGT increased	Recovered
9	AST increased[b]	Recovered
10	Blood creatine phosphokinase increased	Recovered
11	Blood creatine phosphokinase increased[d]	Recovered
12	Hepatitis[b]	Recovered
13	Hypersensitivity[b]	Recovered
14	Abortion spontaneous[e]	Recovered
15	GGT increased[b]	Recovered
16	Multiple drug overdose intentional[b]	Recovered
	Suicide attempt[b]	
17	Abortion spontaneous	Recovered

AST = aspartate aminotransferase; GGT = gamma glutamyl transpeptidase; QD = once daily; SAEs = serious adverse events.

a. Subject outcome rather than SAE outcome.
b. Subject permanently discontinued due to this SAE.
c. Subject temporarily discontinued due to this SAE.
d. One (1) subject had 2 SAEs of blood creatine phosphokinase increased.
e. The SAE of abortion spontaneous was considered to be related to study drug in 1 instance but was listed as related to 'other - probably related to efavirenz' in a second instance.

SAEs reported during the supplemental phase of this study are summarized in Table 44. None of the SAEs were considered treatment-related.

Table 44. Serious Adverse Events (Supplemental Phase)

Subject Serial Number	Seriousness	Suspect Drug/Dose	SAE (MedDRA PT)	Action Taken	Clinical Outcome
1	Hospitalized	Combivir[a]/2 tablet	Umbilical hernia	No action taken	Resolved
		Maraviroc / 600 mg	Umbilical hernia	No action taken	Resolved
2	Hospitalized	Combivir[a]/2 tablet	Injury	No action taken	Resolved
		Combivir[a]/2 tablet	Back injury	No action taken	Resolved
		Maraviroc/300 mg	Injury	No action taken	Resolved
		Maraviroc/300 mg	Back injury	No action taken	Resolved
3	Hospitalized	Combivir[a]/2 tablet	Bronchitis	No action taken	Resolved
		Maraviroc/600 mg	Bronchitis	No action taken	Resolved
4	Subject died	Maraviroc/600 mg	Overdose	No action taken	Fatal
		Truvada/NA	Overdose	No action taken	Fatal

MedDRA = medical dictionary for regulatory activities; N/A = not available or not applicable; PT = preferred term; SAE = serious adverse event.

a. Combivir = zidovudine/lamivudine.

Discontinuations due to AEs: The percentage of subjects who permanently discontinued due to all causality and treatment-related treatment-emergent AEs (TEAE) was lower in the maraviroc 300 mg BID treatment group (27 [7.5%] subjects and 15 [4.2%] subjects, respectively) compared with the efavirenz 600 mg QD treatment group (67 [18.6%] subjects and 47 [13.0%] subjects, respectively).

A similar percentage of subjects temporarily discontinued due to all causality TEAEs in the maraviroc 300 mg BID treatment group compared with the efavirenz 600 mg QD treatment group (20 [5.6%] subjects and 19 [5.3%] subjects, respectively). The TEAEs leading to temporary discontinuation were considered treatment-related by the Investigator for 4 (1.1%) subjects in the maraviroc 300 mg BID treatment group and 8 (2.2%) subjects in the efavirenz 600 mg QD group.

Fourteen (14) subjects (8.0%) discontinued from the maraviroc 300 mg QD treatment group and 3 subjects (2.3%) discontinued from OL maraviroc 300 mg BID due to AEs. The AE(s) leading to discontinuation were considered treatment-related by the Investigator for 8 subjects (4.6%) in the maraviroc 300 mg QD treatment group and for 1 subject (0.6%) on OL maraviroc 300 mg BID.

Details of the TEAEs leading to discontinuation are provided in Table 45, Table 46 and Table 47 for the maraviroc 300 mg BID treatment group, OL phase and for the efavirenz 600 mg QD treatment group.

Table 45. Permanent Discontinuations due to Treatment-Emergent Adverse Events Maraviroc 300 mg BID (All-Causality)

Subject Serial Number	TEAE(s) Leading to Discontinuation (Severity)	Causality
1	Pregnancy (Grade 1)[a]	Other
2	Pregnancy (Grade 2)	Other
3	Nausea (Grade 2)	Study drug
	Fatigue (Grade 2)	Study drug
	Disturbance in attention (Grade 2)	Study drug
	Dizziness (Grade 2)	Study drug
4	Nausea (Grade 2)[a]	Study drug
	Vomiting (Grade 2)[a]	Study drug
	Pyrexia (Grade 3)[a]	Disease under study
5	Pregnancy (Grade 4)[a]	Other
6	Abdominal pain (Grade 4)[a]	Study drug
	Hypertransaminasaemia (Grade 4)[a]	Study drug
	Anorexia (Grade 4)[a]	Study drug
7	ALT increased (Grade 4)	Study drug
	AST increased (Grade 4)	Study drug
8	Myositis (Grade 4)	Study drug
9	ALT increased (Grade 3)	Study drug
10	AST increased (Grade 3)	Study drug
11	ALT increased (Grade 3)	Study drug
12	Metastases to bone (Grade 4)[a]	Disease under study
13	Pulmonary tuberculosis (Grade 1)	Other
14	Hodgkin's disease (Grade 4)[a]	Study drug
15	Hepatitis C (Grade 4)[a]	Other
16	Lipoatrophy (Grade 1)	Concomitant treatment
17	Syncope (Grade 4)[a]	Study drug
18	Pregnancy (Grade 1)	Other
19	Hepatitis C (Grade 2)	Other
20	Tuberculosis (Grade 1)	Disease under study
21	Diffuse large B-cell lymphoma (Grade 4)[a]	Study drug
22	Diarrhoea (Grade 3)	Study drug
	Nausea (Grade 3)	Study drug
	Somnolence (Grade 3)	Study drug
	Anxiety (Grade 3)	Study drug
23	Pregnancy (Grade 1)[a]	Other
24	Depression (Grade 2)	Study drug
25	Transaminases increased (Grade 3)[a]	Study drug
26	Anxiety (Grade 3)	Study drug
	Panic attack (Grade 3)	Study drug
27	ALT increased (Grade 4)[a]	Other
	AST increased (Grade 4)[a]	Other

ALT = alanine transaminase; AST = aspartate transaminase; BID = twice a day; TEAE = treatment-emergent adverse event.

a. Serious adverse event.

Table 46. Permanent Discontinuations due to Adverse Events: (Open-Label Phase)

Subject Serial Number	TEAE(s) Leading to Discontinuation (Severity)	Causality
Maraviroc 300 mg QD		
1	Rash (Grade 2)	Study drug
2	Asthenia (Grade 3)[a]	Study drug
	Pyrexia (Grade 1)[a]	Study drug
	Arthralgia (Grade 2)	Study drug
	Arthralgia (Grade 3)[a]	Study drug
	Myalgia (Grade 2)	Study drug
	Myalgia (Grade 3)[a]	Study drug
	Rash erythematous (Grade 1)[a]	Study drug
3	Depression suicidal (Grade 3)[a]	Other
4	Hepatitis toxic (Grade 4)[a]	Study drug
	Rash (Grade 3)[a]	Study drug
6	Stevens-Johnson syndrome (Grade 4)[a]	Study drug
7	ALT increased (Grade 4)[a]	Concomitant treatment
	ALT increased (Grade 3)	Study drug
8	Pulmonary tuberculosis (Grade 3)	Other
9	Pericardial effusion (Grade 3)[a]	Disease under study
	Ascites (Grade 3)[a]	Disease under study
	Pleural effusion (Grade 3)[a]	Disease under study
10	Depression (Grade 3)	Study drug
11	Disseminated tuberculosis (Grade 4)[a]	Other
12	Nausea (Grade 1)	Study drug
	Anorexia (Grade 1)	Study drug
13	Hepatic enzyme increased (Grade 3)[a]	Disease under study
14	Rash (Grade 1)	Disease under study
	Rash (Grade 2)	Disease under study
15	Salivary hypersecretion (Grade 2)	Study drug
	Vomiting (Grade 2)	Study drug
Maraviroc 300 mg BID		
16	ALT increased (Grade 3)	Study drug
17	Pregnancy	Other
18	Pregnancy	Other

ALT = alanine aminotransferase; BID = twice a day; QD = once daily; TEAE = treatment-emergent adverse events.

a. Serious adverse event.

Table 47. Permanent Discontinuations due to Treatment-Emergent Adverse Events: Efavirenz 600 mg QD (All Causality)

Subject Serial Number	TEAE(s) Leading to Discontinuation (Severity)	Causality
1	Pulmonary tuberculosis (Grade 3)	Other
2	Pregnancy (Grade 1)[a]	Other
3	Pregnancy (Grade 1)[a]	Other
4	Pancytopenia (Grade 3)[a]	Study drug
5	Anaemia (Grade 4)[a]	Study drug
6	Tuberculosis (Grade 1)	Disease under study
7	Pulmonary tuberculosis (Grade 1)	Disease under study
8	Gynaecomastia (Grade 1)	Study drug
9	Anaemia (Grade 3)[a]	Study drug
10	Anaemia (Grade 3)[a]	Other
	Neutropenia (Grade 3)[a]	Other
	Pyrexia (Grade 3)[a]	Other
	Endocarditis (Grade 3)	Disease under study
	Hodgkin's disease (Grade 3)[a]	Disease under study
11	Vision blurred (Grade 1)	Study drug
	Nausea (Grade 1)	Study drug
	Malaise (Grade 1)	Study drug
	Anxiety (Grade 1)	Study drug
	Insomnia (Grade 1)	Study drug
	Rash (Grade 1)	Study drug
12	Pyrexia (Grade 3)[a]	Other
	Castleman's disease (Grade 4)[a]	Disease under study
13	Rash (Grade 4)	Study drug
14	Myocardial infarction (Grade 4)[a]	Study drug
15	Hepatic enzyme increased (Grade 3)[a]	Other
16	Hepatic enzyme increased (Grade 4)[a]	Study drug
	Rash pruritic (Grade 2)[a]	Study drug
17	Pregnancy (Grade 1)[a]	Other
18	Vertigo (Grade 3)	Study drug
	Dizziness (Grade 3)	Study drug
	Confusional state (Grade 3)	Study drug
19	Abdominal pain upper (Grade 3)	Study drug
	Nausea (Grade 1)	Study drug
	Headache (Grade 3)	Study drug
	Confusional state (Grade 3)	Study drug
	Restlessness (Grade 3)	Study drug
20	Blood sodium decreased (Grade 4)[a]	Concomitant treatment
	Rash (Grade 3)[a]	Study drug
21	ALT increased (Grade 2)	Study drug
	AST increased (Grade 3)	Study drug
22	Rash (Grade 2)	Study drug
23	ALT increased (Grade 3)	Study drug
24	Abdominal pain (Grade 2)	Study drug
	Fatigue (Grade 3)	Study drug
	Disturbance in attention (Grade 3)	Study drug
	Abnormal dreams (Grade 3)	Study drug
	Insomnia (Grade 3)	Study drug
25	ALT abnormal (Grade 2)	Study drug
26	AST increased (Grade 3)	Study drug
27	AST increased (Grade 4)[a]	Study drug
28	Rash (Grade 1)	Study drug
29	Lip oedema (Grade 2)	Study drug
	Rash (Grade 3)	Study drug
30	Disturbance in attention (Grade 2)	Study drug
	Dizziness (Grade 2)	Study drug

Table 47. Permanent Discontinuations due to Treatment-Emergent Adverse Events: Efavirenz 600 mg QD (All Causality)

Subject Serial Number	TEAE(s) Leading to Discontinuation (Severity)	Causality
	Nightmare (Grade 2)	Study drug
	Hyperhidrosis (Grade 2)	Study drug
31	Pregnancy (Grade 3)[a]	Other
32	Renal failure (Grade 3)[a]	Concomitant treatment
33	Pulmonary tuberculosis (Grade 2)[a]	Disease under study
34	Hepatitis (Grade 4)[a]	Study drug
35	Cutaneous tuberculosis (Grade 2)	Other
36	Sleep disorder (Grade 2)	Study drug
37	Dizziness (Grade 2)	Study drug
	Headache (Grade 2)	Study drug
	Nightmare (Grade 2)	Study drug
38	Rash generalised (Grade 3)	Study drug
39	Fatigue (Grade 2)	Study drug
	Pulmonary tuberculosis (Grade 4)[a]	Other
	Night sweats (Grade 2)	Study drug
40	Abnormal dreams (Grade 3)	Study drug
	Hallucinations (Grade 3)	Study drug
	Insomnia (Grade 2)	Study drug
41	Pancytopenia (Grade 4)[a]	Other
	Diarrhoea (Grade 2)	Disease under study
	Nausea (Grade 1)	Other
	Asthenia (Grade 2)	Other
	Sepsis (Grade 4)[a]	Other
	Hyperglycaemia (Grade 1)	Other
	Hodgkin's disease (Grade 4)[a]	Other
	Dizziness (Grade 2)	Study drug
	Neuropathy peripheral (Grade 1)	Disease under study
	Psychomotor retardation (Grade 1)	Disease under study
	Renal failure acute (Grade 4)[a]	Other
42	Major depression (Grade 3)	Study drug
43	Non-Hodgkin's lymphoma (Grade 3)[a]	Disease under study
44	Lipodystrophy acquired (Grade 1)	Study drug
45	Vomiting (Grade 1)	Study drug
	Headache (Grade 1)	Study drug
46	Hangover (Grade 1)	Study drug
	Sluggishness (Grade 1)	Study drug
	Emotional distress (Grade 1)	Study drug
47	Hypersensitivity (Grade 4)[a]	Study drug
48	Hypertransaminasaemia (Grade 3)	Study drug
49	Rash (Grade 3)	Study drug
50	Asthenia (Grade 3)	Study drug
	Dizziness (Grade 2)	Study drug
51	Pregnancy (Grade 2)	Other
52	GGT increased (Grade 4)[a]	Study drug
53	ALT increased (Grade 2)[a]	Other
	AST increased (Grade 2)[a]	Other
	Blood creatine phosphokinase increased (Grade 4)[a]	Other
	Blood LDH increased (Grade 4)[a]	Other
54	Nausea (Grade 2)	Study drug
	Dizziness (Grade 2)	Study drug
55	Suicidal ideation (Grade 3)	Study drug
56	Overdose (Grade 4)[a]	Study drug
	Suicide attempt (Grade 4)[a]	Study drug
57	Drug abuse (Grade 1)	Other
58	Diplopia (Grade 3)	Study drug

Table 47. Permanent Discontinuations due to Treatment-Emergent Adverse Events: Efavirenz 600 mg QD (All Causality)

Subject Serial Number	TEAE(s) Leading to Discontinuation (Severity)	Causality
	Diarrhoea (Grade 1)	Study drug
	Nausea (Grade 1)	Study drug
	Dizziness (Grade 3)	Study drug
	Insomnia (Grade 2)	Study drug
59	Pregnancy (Grade 3)[a]	Other
60	Abdominal discomfort (Grade 1)	Disease under study
61	Rash (Grade 1)	Study drug
62	Nausea (Grade 1)	Study drug
	Vomiting (Grade 1)	Study drug
	Dizziness (Grade 1)	Study drug
63	LFT abnormal (Grade 2)	Study drug

ALT = alanine transaminase; AST = aspartate transaminase; GGT = gamma glutamyltransferase; LDH = lactate dehydrogenase; LFT = liver function test; QD = once daily; TEAE = treatment-emergent adverse event.
a. Serious adverse event.

Deaths: A total of 12 subjects died during the study, up to the Week 96 cut-off. Five (5) subjects died while on study drug or within 28 days of study drug discontinuation. Of these, 2 subjects were in the maraviroc 300 mg BID treatment group and 3 subjects were in the efavirenz 600 mg QD treatment group. A further 6 subjects died > 28 days after permanent discontinuation of study drug. Of these, 4 subjects were in the maraviroc 300 mg BID treatment group and 2 subjects were in the efavirenz 600 mg QD treatment group.

One (1) subject in each group was in study, off drug at the time of death. In addition, 1 subject in the efavirenz 600 mg QD treatment group died in a road traffic accident on 25 August 2007. This subject received 422 days of study drug and was permanently discontinued from the study on 21 June 2007, which was the last day the subject received study drug.

One (1) subject who received maraviroc 300 mg QD died due to committing suicide within 28 days of study drug discontinuation. The death was considered by the Investigator to be unrelated to study drug. One (1) more subject who received maraviroc 300 mg QD died >28 days after the End of Treatment due to non-Hodgkin's lymphoma and it was considered unrelated to study drug.

One (1) subject died during the supplemental phase due to a drug overdose which was considered by the Investigator to be unrelated to the study drug.

CONCLUSIONS:

- The antiretroviral activity of maraviroc 300 mg BID in combination with zidovudine/lamivudine did not meet the criterion for non-inferiority to efavirenz 600 mg QD at Week 96 for antiretroviral-naive, CCR5-tropic HIV-1 infected subjects with a viral load of either <400 copies/mL or <50 copies/mL in both the FAS – As Treated population and the PP – As Treated population.

- The difference in the percentage of subjects with viral load <400 copies/mL or <50 copies/mL between the 2 treatment groups at Week 48 did not change through Week 96.

- No difference in the time to loss of virologic response was observed between subjects with a viral load of <400 copies/mL in the maraviroc 300 mg BID and efavirenz 600 mg QD treatment groups. However, the time to loss of virologic response was shorter for subjects with a viral load of <50 copies/mL in the maraviroc 300 mg BID treatment group compared with subjects in the efavirenz 600 mg QD treatment group.

- No difference in the decrease from Baseline to Week 96 in viral load was observed between subjects in the maraviroc 300 mg BID and efavirenz 600 mg QD treatment groups.

- A statistically significant difference in the increase from Baseline in CD4 cell count was observed for subjects in the maraviroc 300 mg BID treatment group compared with subjects in the efavirenz 600 mg QD treatment group at Week 96.

- TAD in $\log_{10}$ transformed viral load from Baseline up to Week 96 was similar for subjects in the maraviroc 300 mg BID and efavirenz 600 mg QD treatment groups.

- A greater proportion of subjects in the maraviroc 300 mg BID treatment group showed genetic and phenotypic resistance to zidovidine and lamivudine at the time of treatment failure compared with subjects in the efavirenz 600 mg QD treatment group.

- A greater proportion of subjects who were CCR5 tropic at Baseline in the maraviroc 300 mg BID treatment group switched to be CXCR4 or dual/mixed tropic at the time of treatment failure compared with subjects in the efavirenz 600 mg QD treatment group. However, median increases in CD4 cell count were higher for subjects of all tropism groups at treatment failure in the maraviroc 300 mg BID treatment group compared with subjects in the efavirenz 600 mg QD treatment group.

- Maraviroc 300 mg BID was safe and well tolerated in treatment-naive subjects over the 96-week study period.

- Maraviroc 300 mg QD and OL maraviroc 300 mg BID were safe and well tolerated in this population of treatment-naive subjects infected with HIV-1, and the AE rates and types reported by subjects randomized to maraviroc 300 mg QD were similar to those reported in other treatment-naive studies.