SUPPLEMENTAL DIGITAL CONTENT

Durable Efficacy and Safety of Raltegravir *versus* Efavirenz When Combined With Tenofovir/Emtricitabine In Treatment-Naive HIV-1 Infected Patients:

Final Five-Year Results From STARTMRK

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Pregnancy Outcomes

Pregnancies were reported in 6 raltegravir recipients and 4 efavirenz recipients during the course of the study, five of whom were lost to follow-up or had elective abortions. The 3 women in the raltegravir group with follow-up information all delivered healthy babies by Caesarian section; the 2 women in the efavirenz group with follow-up information experienced a spontaneous abortion. A congenital cardiac anomaly resulting in neonatal death was reported in the child of a male raltegravir recipient among the 3 men (2 in the raltegravir group) whose female partners were known to have become pregnant while the fathers were receiving study medications.

Table S1. Baseline characteristics

	Raltegravir Group (N = 281)	Efavirenz Group (N = 282)	All Treated Patients (N = 563)
Gender, n (%)			
Male	227 (80.8)	231 (81.9)	458 (81.3)
Female	54 (19.2)	51 (18.1)	105 (18.7)
Race/Ethnicity, n (%)			
White	116 (41.3)	123 (43.6)	239 (42.5)
Black	33 (11.7)	23 (8.2)	56 (9.9)
Asian	36 (12.8)	32 (11.3)	68 (12.1)
Hispanic	60 (21.4)	67 (23.8)	127 (22.6)
Native American	1 (0.4)	1 (0.4)	2 (0.4)
Multiracial	35 (12.5)	36 (12.8)	71 (12.6)
Region, n (%)			
Latin America	99 (35.2)	97 (34.4)	196 (34.8)
Southeast Asia	34 (12.1)	29 (10.3)	63 (11.2)
North America	82 (29.2)	90 (31.9)	172 (30.6)
Europe/Australia	66 (23.5)	66 (23.4)	132 (23.4)
Age, in years			
Mean (SD)	37.6 (9.0)	36.9 (10.0)	37.2 (9.5)
CD4 Cell Count[†]**,** cells/mm^3			
Mean (SD)	218.9 (124.2)	217.4 (133.6)	218.1 (128.8)
Plasma HIV RNA, $\log_{10}$ copies/mL			
Mean (SD)	5.0 (0.6)	5.0 (0.6)	5.0 (0.6)
Investigator-reported History of AIDS, n (%)			
Yes	52 (18.5)	60 (21.3)	112 (19.9)
Stratum, n (%)			
Screening vRNA ≤50,000 copies/mL	75 (26.7)	80 (28.4)	155 (27.5)
Hepatitis B or C	18 (6.4)	16 (5.7)	34 (6.0)
Viral Subtype, n (%)			
Clade B	219 (77.9)	230 (81.6)	449 (79.8)
Non-Clade B	59 (21.0)	47 (16.7)	106 (18.8)
Missing	3 (1.1)	5 (1.8)	8 (1.4)
Baseline Plasma HIV RNA, n (%)			
≤100,000 copies/mL	127 (45.2)	139 (49.3)	266 (47.2)
>100,000 copies/mL	154 (54.8)	143 (50.7)	297 (52.8)
Baseline CD4 Cell Counts, n (%)[†]			
≤50 cells/mm^3	27 (9.6)	31 (11.0)	58 (10.3)
>50 to ≤200 cells/mm^3	104 (37.0)	105 (37.2)	209 (37.1)
>200 cells/mm^3	150 (53.4)	145 (51.4)	295 (52.4)

N = Number of patients in each group; n (%) = number (percent) of patients in each category.
[†] One patient in the efavirenz group had missing results.

Table S2a. Cumulative treatment outcomes for the entire 240-week study

	Raltegravir Group (N=281)	Efavirenz Group (N=282)
HIV RNA level <50 copies/mL [n (%)]	198 (71.0)	171 (61.3)
Mean CD4-cell count change from baseline [cells/mm^3]	374	312
Virologic failure (confirmed vRNA level ≥50 copies/mL) [n (%)]	55 (19.6)	59 (20.9)
Nonresponse [n (%)]	10 (3.6)	24 (8.5)
Rebound [n (%)]	45 (16.0)	35 (12.4)
Death [n (%)]	5 (1.8)	5 (1.8)
Discontinuation due to clinical adverse experiences [n (%)]	14 (5.0)	25 (8.9)
Discontinuation due to laboratory adverse experiences [n (%)]	0 (0.0)	3 (1.1)
Discontinuation due to other reasons [n (%)]†	51 (18.1)	60 (21.3)

†Other reasons for discontinuation are enumerated in **Table S2b**.

Table S2b. Detailed patient accounting with reasons for discontinuations

	Raltegravir Group	Efavirenz Group	Total
	n (%)	n (%)	n (%)
Total Entered	282 (100)	284 (100)	566 (100)
• Never Treated	1 (0.4)	2 (0.7)	3 (0.5)
• **Treated**	281 (99.6)	282 (99.3)	563 (99.5)
o Completed	210 (74.5)	184 (64.8)	394 (69.6)
o **Discontinued Study**	71 (25.2)	98 (34.5)	169 (29.9)
➢ Lack of efficacy	6 (2.1)	10 (3.5)	16 (2.8)
➢ Clinical adverse experience*	14 (5.0)	25 (8.8)	39 (6.9)
➢ Laboratory adverse experience*	0 (0.0)	3 (1.1)	3 (0.5)
➢ Consent withdrawn	5 (1.8)	18 (6.3)	23 (4.1)
➢ Lost to follow-up	12 (4.3)	22 (7.7)	34 (6.0)
➢ Protocol deviation	5 (1.8)	3 (1.1)	8 (1.4)
➢ Declined the extension†	5 (1.8)	6 (2.1)	11 (1.9)
➢ Other‡	24 (8.5)	11 (3.9)	35 (6.2)

*See **Table S2c** for a listing of the adverse events leading to discontinuations in each treatment arm.
†Patients completed original 96-week protocol but did not continue into extension.
‡Including 13 raltegravir and 5 efavirenz recipients who relocated or from terminated study sites.
N (%) = number (percent) of patients in each sub-category.

Table S2c. Adverse events resulting in discontinuations

#	Age/Gender	Adverse Experience	Relative Day of Onset	Relative Day of Discontinuance	Serious?	Drug-related?
Raltegravir Group						
1	34 yr/ M	Anxiety	1	87	N	probably
2	37 yr/ M	Alcohol poisoning and toxicity to various agents	863	863	Y	definitely not
3	42 yr/ M	Memory impairment and mental disorder	87	103	N	probably
4	47 yr/ F	Extrapulmonary tuberculosis	40	40	Y	definitely not
5	43 yr/ M	Hepatitis C	415	511	Y	probably not
6	66 yr/ M	Lung neoplasm malignant	1049	1365	Y	probably not
7	64 yr/ M	Lung cancer metastatic	638	665	Y	definitely not
8	33 yr/ M	Mental disorder	76	90	Y	probably
9	57 yr/ M	Cerebral haemorrhage	90	90	Y	definitely not
10	31 yr/ M	Depression	930	1094	N	probably not
11	35 yr/ M	Pulmonary tuberculosis	671	682	Y	definitely not
12	48 yr/ M	Hepatitis B	110	112	Y	probably not
13	31 yr/ F	Meningitis	48	57	Y	definitely not
14	27 yr/ M	Immune reconstitution syndrome; Kaposi's sarcoma	57	70	Y	probably not
Efavirenz Group						
1	42 yr/ M	Fatigue	2	576	N	probably
2	30 yr/ M	Diarrhoea	1	308	N	possibly
3	30 yr/ M	Drug eruption	9	15	N	probably
4	44 yr/ F	Dystonia	1	1	N	probably
5	63 yr/ M	Decreased appetite, pain, sleep disorder	78	97	N	probably
6	31 yr/ M	Mental disorder	268	337	Y	probably
7	33 yr/ M	Osteopenia	923	1119	N	possibly
8	36 yr/ F	Papule	146	168	N	probably not
9	42 yr/ M	Depression	515	554	N	possibly
10	40 yr/ M	Fatigue, sleep disorder	837	1099	N	probably
11	37 yr/ M	Dermatitis allergic	8	11	N	probably
12	30 yr/ M	Pneumonia, Septic shock	1400	1423	Y	probably not
13	30 yr/ M	Leukaemia	1411	1423	Y	probably not

14	45 yr/ M	Rash macular	11	14	N	possibly
15	25 yr/ M	Hepatitis C	679	711	N	definitely not
16	46 yr/ M	Dizziness	104	106	N	probably
17	36 yr/ F	Anal cancer	961	1000	Y	definitely not
18	23 yr/ M	Rash maculo-papular	2	9	N	probably
19	43 yr/ M	Bone tuberculosis	1018	1060	Y	definitely not
20	44 yr/ M	Anal cancer	189	188	Y	definitely not
21	39 yr/ M	Haemoptysis	1701	1688	Y	definitely not
22	26 yr/ M	Schizoaffective disorder	120	125	Y	possibly
23	51 yr/ M	Kaposi sarcoma	190	190	Y	definitely not
24	36 yr/ F	Anal cancer	961	1000	Y	definitely not
25	34 yr/ M	Pulmonary tuberculosis	358	358	N	Probably not
26	28 yr/ M	Alanine/aspartate aminotransferases increased	58	59	N	Definitely not
27	40 yr/ M	Alanine/aspartate aminotransferases and alkaline phosphatase increased	91	93	N	definite
28	28 yr/ M	Alanine/aspartate aminotransferases increased	758	782	Y	possible
yr, year; F, female; M, male; N, no; Y, yes.						

Table S3. Post-hoc Subgroup Analysis of Week-240 Virologic Response Rates in Patients with Plasma Viremia Below versus Above 250,000 copies/mL at Baseline by Treatment Group Using the Observed-Failure Approach

	Raltegravir Group		Efavirenz Group		Difference in Response Rates
	n/N	% (95% CI)	n/N	% (95% CI)	% (95% CI)
Overall	198/222	89.2 (84.3, 92.9)	171/212	80.7 (74.7, 85.7)	8.5 (1.8, 15.4)
Baseline Plasma vRNA Level (copies/mL)					
≤250,000 copies/mL	145/158	91.8 (86.3, 95.5)	119/150	79.3 (72.0, 85.5)	12.4 (4.7, 20.5)
>250,000 copies/mL	53/64	82.8 (71.3, 91.1)	52/62	83.9 (72.3, 92.0)	-1.1 (-14.4, 12.4)

Table S4. Cumulative summary of genotypic resistance data for patients with vRNA >400 copies/mL at the time of virologic failure

Resistance Frequency by Treatment Group

	Raltegravir (RAL) Group (N=281) n (%)	**Efavirenz (EFV) Group** (N=282) n (%)
Virologic Failure (confirmed vRNA level ≥50 copies/mL)	55 (19.6)	59 (20.9)
Resistance data available (vRNA level >400 copies/mL)	23 (8.2)	20 (7.1)
• RAL or EFV Resistance Alone	1	7
• RAL or EFV Resistance and NRTI Resistance	3	3
• NRTI Resistance Alone	3	2

Number (%) of Evaluable Raltegravir Recipients[§] with Identified Viral Integrase Mutations

	Raltegravir (RAL) Group (N=281)	
	Non-Response (n=2)	**Viral Rebound** (n=16)
With Mutation at Amino Acid 143, 148 or 155	2 (100)	2 (12.5)
With Mutation at Amino Acid 143	0 (0)	2 (12.5)
With Mutation at Amino Acid 148	2 (100)	0 (0)
With Mutation at Amino Acid 155	0 (0)	0 (0)
With No Mutation at Either Amino Acid 143, 148 or 155	0 (0)	14 (87.5)
With Other Known RAL Resistance Mutations	0 (0)	1 (6.3)
With No Other Known RAL Resistance Mutations	0 (0)	13 (81.3)

[§]There were 5 raltegravir recipients who experienced virologic failure where the integrase gene could not be amplified.

Table S5. Number (%) of patients with specific moderate-to-severe clinical adverse events irrespective of frequency or causality in either treatment group

Number (%) of Patients With Specific Clinical Adverse Experiences
(Incidence >0% in One or More Treatment Groups) by System Organ Class - All Events - Moderate or Severe - Double-Blind Phase, All Available Data

	Raltegravir 400 mg b.i.d. (N = 281)		Efavirenz 600 mg q.h.s. (N = 282)		Total (N = 563)	
	n	(%)	n	(%)	n	(%)
Patients With One Or More Adverse Experiences	201	(71.5)	222	(78.7)	423	(75.1)
Patients With No Adverse Experience	80	(28.5)	60	(21.3)	140	(24.9)
Blood And Lymphatic System Disorders	11	(3.9)	6	(2.1)	17	(3.0)
Anaemia	5	(1.8)	2	(0.7)	7	(1.2)
Eosinophilia	0	(0.0)	1	(0.4)	1	(0.2)
Febrile Neutropenia	0	(0.0)	1	(0.4)	1	(0.2)
Iron Deficiency Anaemia	1	(0.4)	1	(0.4)	2	(0.4)
Lymph Node Pain	1	(0.4)	0	(0.0)	1	(0.2)
Lymphadenopathy	5	(1.8)	0	(0.0)	5	(0.9)
Microcytic Anaemia	1	(0.4)	0	(0.0)	1	(0.2)
Neutropenia	2	(0.7)	1	(0.4)	3	(0.5)
Pancytopenia	1	(0.4)	0	(0.0)	1	(0.2)
Cardiac Disorders	6	(2.1)	5	(1.8)	11	(2.0)
Acute Myocardial Infarction	0	(0.0)	1	(0.4)	1	(0.2)
Cardiac Failure	1	(0.4)	0	(0.0)	1	(0.2)
Coronary Artery Disease	0	(0.0)	1	(0.4)	1	(0.2)
Dilatation Ventricular	0	(0.0)	1	(0.4)	1	(0.2)
Palpitations	2	(0.7)	1	(0.4)	3	(0.5)
Sinus Bradycardia	1	(0.4)	0	(0.0)	1	(0.2)
Tachycardia	2	(0.7)	1	(0.4)	3	(0.5)
Congenital, Familial And Genetic Disorders	2	(0.7)	2	(0.7)	4	(0.7)

Number (%) of Patients With Specific Clinical Adverse Experiences
(Incidence >0% in One or More Treatment Groups) by System Organ Class - All Events - Moderate or Severe - Double-Blind Phase, All Available Data

	Raltegravir 400 mg b.i.d. (N = 281)		Efavirenz 600 mg q.h.s. (N = 282)		Total (N = 563)	
	n	(%)	n	(%)	n	(%)
Congenital, Familial And Genetic Disorders	2	(0.7)	2	(0.7)	4	(0.7)
Branchial Cleft Cyst	0	(0.0)	1	(0.4)	1	(0.2)
Cystic Lymphangioma	1	(0.4)	0	(0.0)	1	(0.2)
Hydrocele	0	(0.0)	1	(0.4)	1	(0.2)
Keratosis Follicular	1	(0.4)	0	(0.0)	1	(0.2)
Ear And Labyrinth Disorders	9	(3.2)	5	(1.8)	14	(2.5)
Ear Discomfort	1	(0.4)	0	(0.0)	1	(0.2)
Ear Pain	1	(0.4)	0	(0.0)	1	(0.2)
Ear Pruritus	1	(0.4)	0	(0.0)	1	(0.2)
Hearing Impaired	1	(0.4)	0	(0.0)	1	(0.2)
Motion Sickness	1	(0.4)	1	(0.4)	2	(0.4)
Neurosensory Hypoacusis	0	(0.0)	1	(0.4)	1	(0.2)
Tinnitus	1	(0.4)	0	(0.0)	1	(0.2)
Tympanic Membrane Perforation	1	(0.4)	0	(0.0)	1	(0.2)
Vertigo	2	(0.7)	3	(1.1)	5	(0.9)
Endocrine Disorders	2	(0.7)	4	(1.4)	6	(1.1)
Hyperthyroidism	1	(0.4)	0	(0.0)	1	(0.2)
Hypogonadism	1	(0.4)	3	(1.1)	4	(0.7)
Thyroiditis	0	(0.0)	1	(0.4)	1	(0.2)
Eye Disorders	6	(2.1)	7	(2.5)	13	(2.3)
Cataract	1	(0.4)	0	(0.0)	1	(0.2)
Chalazion	1	(0.4)	0	(0.0)	1	(0.2)

Number (%) of Patients With Specific Clinical Adverse Experiences
(Incidence >0% in One or More Treatment Groups) by System Organ Class - All Events - Moderate or Severe - Double-Blind Phase, All Available Data

	Raltegravir 400 mg b.i.d. (N = 281)		Efavirenz 600 mg q.h.s. (N = 282)		Total (N = 563)	
	n	(%)	n	(%)	n	(%)
Eye Disorders	6	(2.1)	7	(2.5)	13	(2.3)
Conjunctival Haemorrhage	0	(0.0)	1	(0.4)	1	(0.2)
Conjunctivitis	1	(0.4)	3	(1.1)	4	(0.7)
Conjunctivitis Allergic	1	(0.4)	2	(0.7)	3	(0.5)
Glaucoma	1	(0.4)	0	(0.0)	1	(0.2)
Iritis	1	(0.4)	0	(0.0)	1	(0.2)
Photophobia	1	(0.4)	0	(0.0)	1	(0.2)
Uveitis	0	(0.0)	1	(0.4)	1	(0.2)
Vision Blurred	0	(0.0)	1	(0.4)	1	(0.2)
Gastrointestinal Disorders	68	(24.2)	74	(26.2)	142	(25.2)
Abdominal Distension	2	(0.7)	4	(1.4)	6	(1.1)
Abdominal Mass	0	(0.0)	1	(0.4)	1	(0.2)
Abdominal Pain	13	(4.6)	8	(2.8)	21	(3.7)
Abdominal Pain Lower	1	(0.4)	0	(0.0)	1	(0.2)
Abdominal Pain Upper	3	(1.1)	5	(1.8)	8	(1.4)
Anal Fistula	2	(0.7)	2	(0.7)	4	(0.7)
Anal Polyp	0	(0.0)	1	(0.4)	1	(0.2)
Anal Ulcer	1	(0.4)	0	(0.0)	1	(0.2)
Anogenital Dysplasia	1	(0.4)	0	(0.0)	1	(0.2)
Anorectal Varices	1	(0.4)	0	(0.0)	1	(0.2)
Bowel Movement Irregularity	0	(0.0)	1	(0.4)	1	(0.2)
Colitis	2	(0.7)	2	(0.7)	4	(0.7)

Number (%) of Patients With Specific Clinical Adverse Experiences
(Incidence >0% in One or More Treatment Groups) by System Organ Class - All Events - Moderate or Severe - Double-Blind Phase, All Available Data

	Raltegravir 400 mg b.i.d. (N = 281)		Efavirenz 600 mg q.h.s. (N = 282)		Total (N = 563)	
	n	(%)	n	(%)	n	(%)
Gastrointestinal Disorders	68	(24.2)	74	(26.2)	142	(25.2)
Constipation	0	(0.0)	4	(1.4)	4	(0.7)
Dental Caries	1	(0.4)	1	(0.4)	2	(0.4)
Diarrhoea	18	(6.4)	21	(7.4)	39	(6.9)
Diverticulum Intestinal	1	(0.4)	0	(0.0)	1	(0.2)
Dry Mouth	0	(0.0)	1	(0.4)	1	(0.2)
Duodenal Ulcer	1	(0.4)	0	(0.0)	1	(0.2)
Dyspepsia	4	(1.4)	3	(1.1)	7	(1.2)
Dysphagia	1	(0.4)	1	(0.4)	2	(0.4)
Enteritis	1	(0.4)	1	(0.4)	2	(0.4)
Erosive Duodenitis	1	(0.4)	0	(0.0)	1	(0.2)
Flatulence	3	(1.1)	4	(1.4)	7	(1.2)
Food Poisoning	1	(0.4)	2	(0.7)	3	(0.5)
Functional Gastrointestinal Disorder	0	(0.0)	1	(0.4)	1	(0.2)
Gastritis	2	(0.7)	5	(1.8)	7	(1.2)
Gastrointestinal Disorder	0	(0.0)	1	(0.4)	1	(0.2)
Gastrooesophageal Reflux Disease	5	(1.8)	3	(1.1)	8	(1.4)
Gingivitis	1	(0.4)	3	(1.1)	4	(0.7)
Haematochezia	2	(0.7)	1	(0.4)	3	(0.5)
Haemorrhoids	3	(1.1)	4	(1.4)	7	(1.2)
Inguinal Hernia	0	(0.0)	1	(0.4)	1	(0.2)
Intestinal Mass	1	(0.4)	0	(0.0)	1	(0.2)

Number (%) of Patients With Specific Clinical Adverse Experiences
(Incidence >0% in One or More Treatment Groups) by System Organ Class - All Events - Moderate or Severe - Double-Blind Phase, All Available Data

	Raltegravir 400 mg b.i.d. (N = 281)		Efavirenz 600 mg q.h.s. (N = 282)		Total (N = 563)	
	n	(%)	n	(%)	n	(%)
Gastrointestinal Disorders	68	(24.2)	74	(26.2)	142	(25.2)
Lower Gastrointestinal Haemorrhage	1	(0.4)	0	(0.0)	1	(0.2)
Nausea	17	(6.0)	13	(4.6)	30	(5.3)
Odynophagia	0	(0.0)	1	(0.4)	1	(0.2)
Oesophageal Spasm	0	(0.0)	1	(0.4)	1	(0.2)
Oesophagitis	2	(0.7)	0	(0.0)	2	(0.4)
Oral Pain	0	(0.0)	1	(0.4)	1	(0.2)
Pancreatitis	2	(0.7)	1	(0.4)	3	(0.5)
Pancreatitis Acute	1	(0.4)	0	(0.0)	1	(0.2)
Peptic Ulcer	1	(0.4)	0	(0.0)	1	(0.2)
Periodontal Disease	0	(0.0)	1	(0.4)	1	(0.2)
Periodontitis	0	(0.0)	2	(0.7)	2	(0.4)
Proctalgia	1	(0.4)	2	(0.7)	3	(0.5)
Proctitis	2	(0.7)	1	(0.4)	3	(0.5)
Rectal Haemorrhage	1	(0.4)	1	(0.4)	2	(0.4)
Salivary Gland Calculus	0	(0.0)	1	(0.4)	1	(0.2)
Toothache	2	(0.7)	4	(1.4)	6	(1.1)
Umbilical Hernia	1	(0.4)	0	(0.0)	1	(0.2)
Vomiting	6	(2.1)	6	(2.1)	12	(2.1)
General Disorders And Administration Site Conditions	39	(13.9)	46	(16.3)	85	(15.1)
Asthenia	8	(2.8)	5	(1.8)	13	(2.3)
Chest Discomfort	1	(0.4)	0	(0.0)	1	(0.2)

Number (%) of Patients With Specific Clinical Adverse Experiences
(Incidence >0% in One or More Treatment Groups) by System Organ Class - All Events - Moderate or Severe - Double-Blind Phase, All Available Data

	Raltegravir 400 mg b.i.d. (N = 281)		Efavirenz 600 mg q.h.s. (N = 282)		Total (N = 563)	
	n	(%)	n	(%)	n	(%)
General Disorders And Administration Site Conditions	39	(13.9)	46	(16.3)	85	(15.1)
Chest Pain	2	(0.7)	3	(1.1)	5	(0.9)
Chills	3	(1.1)	3	(1.1)	6	(1.1)
Early Satiety	0	(0.0)	1	(0.4)	1	(0.2)
Fatigue	10	(3.6)	10	(3.5)	20	(3.6)
Feeling Abnormal	1	(0.4)	1	(0.4)	2	(0.4)
Influenza Like Illness	2	(0.7)	5	(1.8)	7	(1.2)
Irritability	0	(0.0)	1	(0.4)	1	(0.2)
Local Swelling	1	(0.4)	1	(0.4)	2	(0.4)
Localised Oedema	0	(0.0)	1	(0.4)	1	(0.2)
Malaise	0	(0.0)	2	(0.7)	2	(0.4)
Non-Cardiac Chest Pain	0	(0.0)	1	(0.4)	1	(0.2)
Oedema Peripheral	2	(0.7)	3	(1.1)	5	(0.9)
Pain	7	(2.5)	2	(0.7)	9	(1.6)
Pseudocyst	1	(0.4)	0	(0.0)	1	(0.2)
Pyrexia	17	(6.0)	14	(5.0)	31	(5.5)
Submandibular Mass	1	(0.4)	0	(0.0)	1	(0.2)
Thirst	1	(0.4)	0	(0.0)	1	(0.2)
Ulcer	1	(0.4)	0	(0.0)	1	(0.2)
Hepatobiliary Disorders	8	(2.8)	1	(0.4)	9	(1.6)
Biliary Colic	1	(0.4)	0	(0.0)	1	(0.2)
Cholangitis	1	(0.4)	0	(0.0)	1	(0.2)

Number (%) of Patients With Specific Clinical Adverse Experiences
(Incidence >0% in One or More Treatment Groups) by System Organ Class - All Events - Moderate or Severe - Double-Blind Phase, All Available Data

	Raltegravir 400 mg b.i.d. (N = 281)		Efavirenz 600 mg q.h.s. (N = 282)		Total (N = 563)	
	n	(%)	n	(%)	n	(%)
Hepatobiliary Disorders	8	(2.8)	1	(0.4)	9	(1.6)
Cholecystitis	1	(0.4)	0	(0.0)	1	(0.2)
Cholecystitis Chronic	1	(0.4)	0	(0.0)	1	(0.2)
Hepatic Steatosis	1	(0.4)	0	(0.0)	1	(0.2)
Hepatitis	1	(0.4)	1	(0.4)	2	(0.4)
Hepatitis Alcoholic	1	(0.4)	0	(0.0)	1	(0.2)
Jaundice	1	(0.4)	0	(0.0)	1	(0.2)
Immune System Disorders	10	(3.6)	5	(1.8)	15	(2.7)
Allergy To Arthropod Bite	0	(0.0)	1	(0.4)	1	(0.2)
Drug Hypersensitivity	2	(0.7)	2	(0.7)	4	(0.7)
Immune Reconstitution Syndrome	5	(1.8)	2	(0.7)	7	(1.2)
Seasonal Allergy	3	(1.1)	0	(0.0)	3	(0.5)
Infections And Infestations	118	(42.0)	123	(43.6)	241	(42.8)
Abdominal Abscess	1	(0.4)	0	(0.0)	1	(0.2)
Abscess Jaw	1	(0.4)	0	(0.0)	1	(0.2)
Abscess Limb	1	(0.4)	1	(0.4)	2	(0.4)
Acarodermatitis	5	(1.8)	4	(1.4)	9	(1.6)
Acute Sinusitis	4	(1.4)	2	(0.7)	6	(1.1)
Acute Tonsillitis	1	(0.4)	0	(0.0)	1	(0.2)
Anal Abscess	0	(0.0)	1	(0.4)	1	(0.2)
Appendicitis	0	(0.0)	4	(1.4)	4	(0.7)
Bacteraemia	0	(0.0)	1	(0.4)	1	(0.2)

Number (%) of Patients With Specific Clinical Adverse Experiences
(Incidence >0% in One or More Treatment Groups) by System Organ Class - All Events - Moderate or Severe - Double-Blind Phase, All Available Data

	Raltegravir 400 mg b.i.d. (N = 281)		Efavirenz 600 mg q.h.s. (N = 282)		Total (N = 563)	
	n	(%)	n	(%)	n	(%)
Infections And Infestations	118	(42.0)	123	(43.6)	241	(42.8)
Bacterial Pyelonephritis	0	(0.0)	1	(0.4)	1	(0.2)
Bone Tuberculosis	0	(0.0)	1	(0.4)	1	(0.2)
Bronchitis	15	(5.3)	13	(4.6)	28	(5.0)
Bronchopneumonia	1	(0.4)	0	(0.0)	1	(0.2)
Cellulitis	1	(0.4)	4	(1.4)	5	(0.9)
Chlamydial Infection	0	(0.0)	3	(1.1)	3	(0.5)
Chronic Sinusitis	1	(0.4)	0	(0.0)	1	(0.2)
Cryptosporidiosis Infection	0	(0.0)	1	(0.4)	1	(0.2)
Cystitis	1	(0.4)	1	(0.4)	2	(0.4)
Cytomegalovirus Colitis	0	(0.0)	1	(0.4)	1	(0.2)
Cytomegalovirus Viraemia	1	(0.4)	0	(0.0)	1	(0.2)
Dengue Fever	1	(0.4)	1	(0.4)	2	(0.4)
Dermatophytosis	0	(0.0)	1	(0.4)	1	(0.2)
Diarrhoea Infectious	1	(0.4)	0	(0.0)	1	(0.2)
Ear Infection	2	(0.7)	4	(1.4)	6	(1.1)
Enterocolitis Infectious	1	(0.4)	0	(0.0)	1	(0.2)
Erysipelas	1	(0.4)	1	(0.4)	2	(0.4)
Extrapulmonary Tuberculosis	1	(0.4)	0	(0.0)	1	(0.2)
Eye Infection	0	(0.0)	2	(0.7)	2	(0.4)
Folliculitis	3	(1.1)	2	(0.7)	5	(0.9)
Fungal Skin Infection	1	(0.4)	1	(0.4)	2	(0.4)

Number (%) of Patients With Specific Clinical Adverse Experiences
(Incidence >0% in One or More Treatment Groups) by System Organ Class - All Events - Moderate or Severe - Double-Blind Phase, All Available Data

	Raltegravir 400 mg b.i.d. (N = 281)		Efavirenz 600 mg q.h.s. (N = 282)		Total (N = 563)	
	n	(%)	n	(%)	n	(%)
Infections And Infestations	118	(42.0)	123	(43.6)	241	(42.8)
Furuncle	0	(0.0)	1	(0.4)	1	(0.2)
Gastroenteritis	8	(2.8)	8	(2.8)	16	(2.8)
Gastroenteritis Bacterial	0	(0.0)	1	(0.4)	1	(0.2)
Gastroenteritis Viral	0	(0.0)	5	(1.8)	5	(0.9)
Genital Herpes	5	(1.8)	6	(2.1)	11	(2.0)
Genitourinary Chlamydia Infection	0	(0.0)	1	(0.4)	1	(0.2)
Giardiasis	0	(0.0)	1	(0.4)	1	(0.2)
Gonorrhoea	2	(0.7)	1	(0.4)	3	(0.5)
H1N1 Influenza	1	(0.4)	0	(0.0)	1	(0.2)
HIV Wasting Syndrome	0	(0.0)	1	(0.4)	1	(0.2)
Helicobacter Infection	1	(0.4)	0	(0.0)	1	(0.2)
Hepatitis A	1	(0.4)	0	(0.0)	1	(0.2)
Hepatitis C	2	(0.7)	2	(0.7)	4	(0.7)
Herpes Dermatitis	1	(0.4)	0	(0.0)	1	(0.2)
Herpes Simplex	3	(1.1)	2	(0.7)	5	(0.9)
Herpes Zoster	10	(3.6)	11	(3.9)	21	(3.7)
Herpes Zoster Ophthalmic	0	(0.0)	1	(0.4)	1	(0.2)
Hordeolum	0	(0.0)	2	(0.7)	2	(0.4)
Impetigo	1	(0.4)	1	(0.4)	2	(0.4)
Infected Skin Ulcer	1	(0.4)	0	(0.0)	1	(0.2)
Infectious Mononucleosis	0	(0.0)	1	(0.4)	1	(0.2)

Number (%) of Patients With Specific Clinical Adverse Experiences
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	Raltegravir 400 mg b.i.d. (N = 281)		Efavirenz 600 mg q.h.s. (N = 282)		Total (N = 563)	
	n	(%)	n	(%)	n	(%)
Infections And Infestations	118	(42.0)	123	(43.6)	241	(42.8)
Influenza	11	(3.9)	11	(3.9)	22	(3.9)
Labyrinthitis	0	(0.0)	1	(0.4)	1	(0.2)
Latent Syphilis	1	(0.4)	0	(0.0)	1	(0.2)
Localised Infection	1	(0.4)	1	(0.4)	2	(0.4)
Lung Infection	0	(0.0)	1	(0.4)	1	(0.2)
Lymph Node Abscess	1	(0.4)	0	(0.0)	1	(0.2)
Lymphangitis	0	(0.0)	1	(0.4)	1	(0.2)
Meningitis	1	(0.4)	0	(0.0)	1	(0.2)
Meningitis Aseptic	1	(0.4)	0	(0.0)	1	(0.2)
Mycobacterium Avium Complex Infection	1	(0.4)	0	(0.0)	1	(0.2)
Nail Infection	0	(0.0)	1	(0.4)	1	(0.2)
Nasal Abscess	1	(0.4)	0	(0.0)	1	(0.2)
Nasopharyngitis	7	(2.5)	10	(3.5)	17	(3.0)
Neurosyphilis	1	(0.4)	0	(0.0)	1	(0.2)
Oesophageal Candidiasis	0	(0.0)	1	(0.4)	1	(0.2)
Onychomycosis	3	(1.1)	2	(0.7)	5	(0.9)
Oral Candidiasis	1	(0.4)	1	(0.4)	2	(0.4)
Oral Herpes	1	(0.4)	2	(0.7)	3	(0.5)
Orchitis	0	(0.0)	1	(0.4)	1	(0.2)
Osteomyelitis	1	(0.4)	0	(0.0)	1	(0.2)
Otitis Externa	1	(0.4)	2	(0.7)	3	(0.5)

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	n	(%)	n	(%)	n	(%)
Infections And Infestations	118	(42.0)	123	(43.6)	241	(42.8)
Otitis Media	5	(1.8)	3	(1.1)	8	(1.4)
Papilloma Viral Infection	1	(0.4)	0	(0.0)	1	(0.2)
Parasitic Gastroenteritis	0	(0.0)	1	(0.4)	1	(0.2)
Penicilliosis	0	(0.0)	1	(0.4)	1	(0.2)
Pharyngitis	11	(3.9)	6	(2.1)	17	(3.0)
Pharyngitis Streptococcal	1	(0.4)	0	(0.0)	1	(0.2)
Pharyngotonsillitis	0	(0.0)	2	(0.7)	2	(0.4)
Pneumocystis Jiroveci Pneumonia	0	(0.0)	1	(0.4)	1	(0.2)
Pneumonia	5	(1.8)	9	(3.2)	14	(2.5)
Pneumonia Bacterial	0	(0.0)	1	(0.4)	1	(0.2)
Pneumonia Primary Atypical	1	(0.4)	0	(0.0)	1	(0.2)
Postoperative Wound Infection	1	(0.4)	0	(0.0)	1	(0.2)
Primary Syphilis	0	(0.0)	1	(0.4)	1	(0.2)
Proctitis Herpes	1	(0.4)	0	(0.0)	1	(0.2)
Pulmonary Tuberculosis	1	(0.4)	0	(0.0)	1	(0.2)
Pulpitis Dental	0	(0.0)	1	(0.4)	1	(0.2)
Pyelonephritis	0	(0.0)	1	(0.4)	1	(0.2)
Pyelonephritis Acute	1	(0.4)	0	(0.0)	1	(0.2)
Rash Pustular	1	(0.4)	1	(0.4)	2	(0.4)
Respiratory Tract Infection	1	(0.4)	2	(0.7)	3	(0.5)
Respiratory Tract Infection Viral	1	(0.4)	0	(0.0)	1	(0.2)

Number (%) of Patients With Specific Clinical Adverse Experiences
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	Raltegravir 400 mg b.i.d. (N = 281)		Efavirenz 600 mg q.h.s. (N = 282)		Total (N = 563)	
	n	(%)	n	(%)	n	(%)
Infections And Infestations	118	(42.0)	123	(43.6)	241	(42.8)
Rhinitis	2	(0.7)	2	(0.7)	4	(0.7)
Rocky Mountain Spotted Fever	0	(0.0)	1	(0.4)	1	(0.2)
Secondary Syphilis	5	(1.8)	0	(0.0)	5	(0.9)
Sepsis	1	(0.4)	0	(0.0)	1	(0.2)
Septic Shock	0	(0.0)	1	(0.4)	1	(0.2)
Sinusitis	12	(4.3)	15	(5.3)	27	(4.8)
Skin Infection	0	(0.0)	1	(0.4)	1	(0.2)
Subcutaneous Abscess	3	(1.1)	4	(1.4)	7	(1.2)
Syphilis	6	(2.1)	9	(3.2)	15	(2.7)
Tinea Cruris	0	(0.0)	1	(0.4)	1	(0.2)
Tinea Pedis	4	(1.4)	0	(0.0)	4	(0.7)
Tinea Versicolour	1	(0.4)	0	(0.0)	1	(0.2)
Tonsillitis	6	(2.1)	3	(1.1)	9	(1.6)
Tooth Abscess	1	(0.4)	6	(2.1)	7	(1.2)
Tooth Infection	0	(0.0)	1	(0.4)	1	(0.2)
Tracheitis	1	(0.4)	0	(0.0)	1	(0.2)
Tracheobronchitis	1	(0.4)	2	(0.7)	3	(0.5)
Tuberculosis	1	(0.4)	1	(0.4)	2	(0.4)
Tuberculosis Gastrointestinal	2	(0.7)	0	(0.0)	2	(0.4)
Upper Respiratory Tract Infection	17	(6.0)	14	(5.0)	31	(5.5)
Urethritis	3	(1.1)	1	(0.4)	4	(0.7)

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	n	(%)	n	(%)	n	(%)
Infections And Infestations	118	(42.0)	123	(43.6)	241	(42.8)
Urethritis Gonococcal	1	(0.4)	0	(0.0)	1	(0.2)
Urinary Tract Infection	2	(0.7)	10	(3.5)	12	(2.1)
Vaginal Infection	0	(0.0)	1	(0.4)	1	(0.2)
Vaginitis Bacterial	1	(0.4)	0	(0.0)	1	(0.2)
Varicella	0	(0.0)	1	(0.4)	1	(0.2)
Vestibular Neuronitis	0	(0.0)	1	(0.4)	1	(0.2)
Viral Infection	1	(0.4)	0	(0.0)	1	(0.2)
Viral Rash	0	(0.0)	1	(0.4)	1	(0.2)
Viral Rhinitis	1	(0.4)	0	(0.0)	1	(0.2)
Viral Upper Respiratory Tract Infection	2	(0.7)	1	(0.4)	3	(0.5)
Vulvovaginal Candidiasis	1	(0.4)	0	(0.0)	1	(0.2)
Wound Infection	0	(0.0)	1	(0.4)	1	(0.2)
Injury, Poisoning And Procedural Complications	28	(10.0)	32	(11.3)	60	(10.7)
Accidental Exposure	0	(0.0)	1	(0.4)	1	(0.2)
Alcohol Poisoning	1	(0.4)	1	(0.4)	2	(0.4)
Animal Bite	2	(0.7)	0	(0.0)	2	(0.4)
Ankle Fracture	0	(0.0)	1	(0.4)	1	(0.2)
Arthropod Bite	2	(0.7)	0	(0.0)	2	(0.4)
Cervical Vertebral Fracture	1	(0.4)	0	(0.0)	1	(0.2)
Chemical Poisoning	1	(0.4)	0	(0.0)	1	(0.2)
Chest Injury	0	(0.0)	1	(0.4)	1	(0.2)

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	n	(%)	n	(%)	n	(%)
Injury, Poisoning And Procedural Complications	28	(10.0)	32	(11.3)	60	(10.7)
Clavicle Fracture	1	(0.4)	1	(0.4)	2	(0.4)
Contusion	1	(0.4)	4	(1.4)	5	(0.9)
Corneal Abrasion	1	(0.4)	1	(0.4)	2	(0.4)
Epicondylitis	1	(0.4)	0	(0.0)	1	(0.2)
Excoriation	1	(0.4)	2	(0.7)	3	(0.5)
Fall	0	(0.0)	1	(0.4)	1	(0.2)
Femoral Neck Fracture	0	(0.0)	1	(0.4)	1	(0.2)
Fibula Fracture	0	(0.0)	1	(0.4)	1	(0.2)
Foot Fracture	0	(0.0)	1	(0.4)	1	(0.2)
Hand Fracture	2	(0.7)	1	(0.4)	3	(0.5)
Humerus Fracture	1	(0.4)	0	(0.0)	1	(0.2)
Injury	1	(0.4)	0	(0.0)	1	(0.2)
Intentional Overdose	1	(0.4)	0	(0.0)	1	(0.2)
Joint Dislocation	0	(0.0)	3	(1.1)	3	(0.5)
Joint Injury	0	(0.0)	3	(1.1)	3	(0.5)
Laceration	3	(1.1)	4	(1.4)	7	(1.2)
Ligament Rupture	1	(0.4)	0	(0.0)	1	(0.2)
Ligament Sprain	0	(0.0)	2	(0.7)	2	(0.4)
Limb Injury	1	(0.4)	0	(0.0)	1	(0.2)
Lip Injury	1	(0.4)	0	(0.0)	1	(0.2)
Lower Limb Fracture	1	(0.4)	0	(0.0)	1	(0.2)

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	n	(%)	n	(%)	n	(%)
Injury, Poisoning And Procedural Complications	28	(10.0)	32	(11.3)	60	(10.7)
Multiple Injuries	0	(0.0)	1	(0.4)	1	(0.2)
Muscle Strain	1	(0.4)	2	(0.7)	3	(0.5)
Open Wound	1	(0.4)	0	(0.0)	1	(0.2)
Post Lumbar Puncture Syndrome	1	(0.4)	0	(0.0)	1	(0.2)
Procedural Pain	0	(0.0)	2	(0.7)	2	(0.4)
Radius Fracture	0	(0.0)	1	(0.4)	1	(0.2)
Rib Fracture	1	(0.4)	2	(0.7)	3	(0.5)
Road Traffic Accident	1	(0.4)	0	(0.0)	1	(0.2)
Soft Tissue Injury	0	(0.0)	1	(0.4)	1	(0.2)
Spinal Column Injury	1	(0.4)	0	(0.0)	1	(0.2)
Subdural Haematoma	1	(0.4)	0	(0.0)	1	(0.2)
Toxicity To Various Agents	1	(0.4)	0	(0.0)	1	(0.2)
Upper Limb Fracture	0	(0.0)	1	(0.4)	1	(0.2)
Wound	1	(0.4)	1	(0.4)	2	(0.4)
Investigations	9	(3.2)	8	(2.8)	17	(3.0)
Blood Pressure Increased	0	(0.0)	2	(0.7)	2	(0.4)
Cardiac Murmur	1	(0.4)	0	(0.0)	1	(0.2)
Helicobacter Test Positive	0	(0.0)	1	(0.4)	1	(0.2)
Platelet Count Decreased	1	(0.4)	0	(0.0)	1	(0.2)
Tuberculin Test Positive	1	(0.4)	0	(0.0)	1	(0.2)
Waist Circumference Increased	0	(0.0)	1	(0.4)	1	(0.2)

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	n	(%)	n	(%)	n	(%)
Investigations	9	(3.2)	8	(2.8)	17	(3.0)
Weight Decreased	5	(1.8)	4	(1.4)	9	(1.6)
Weight Increased	1	(0.4)	0	(0.0)	1	(0.2)
Metabolism And Nutrition Disorders	15	(5.3)	22	(7.8)	37	(6.6)
Abnormal Loss Of Weight	0	(0.0)	1	(0.4)	1	(0.2)
Body Fat Disorder	1	(0.4)	0	(0.0)	1	(0.2)
Decreased Appetite	5	(1.8)	5	(1.8)	10	(1.8)
Dehydration	1	(0.4)	0	(0.0)	1	(0.2)
Diabetes Mellitus	1	(0.4)	2	(0.7)	3	(0.5)
Dyslipidaemia	0	(0.0)	1	(0.4)	1	(0.2)
Gout	1	(0.4)	1	(0.4)	2	(0.4)
Hypercholesterolaemia	3	(1.1)	4	(1.4)	7	(1.2)
Hyperglycaemia	1	(0.4)	1	(0.4)	2	(0.4)
Hyperlipidaemia	1	(0.4)	5	(1.8)	6	(1.1)
Hyperphagia	1	(0.4)	0	(0.0)	1	(0.2)
Hypertriglyceridaemia	0	(0.0)	3	(1.1)	3	(0.5)
Increased Appetite	1	(0.4)	0	(0.0)	1	(0.2)
Lactose Intolerance	0	(0.0)	1	(0.4)	1	(0.2)
Overweight	1	(0.4)	0	(0.0)	1	(0.2)
Vitamin K Deficiency	0	(0.0)	1	(0.4)	1	(0.2)
Musculoskeletal And Connective Tissue Disorders	43	(15.3)	45	(16.0)	88	(15.6)
Arthralgia	7	(2.5)	14	(5.0)	21	(3.7)

Number (%) of Patients With Specific Clinical Adverse Experiences
(Incidence >0% in One or More Treatment Groups) by System Organ Class - All Events - Moderate or Severe - Double-Blind Phase, All Available Data

	Raltegravir 400 mg b.i.d. (N = 281)		Efavirenz 600 mg q.h.s. (N = 282)		Total (N = 563)	
	n	(%)	n	(%)	n	(%)
Musculoskeletal And Connective Tissue Disorders	43	(15.3)	45	(16.0)	88	(15.6)
Arthritis	1	(0.4)	1	(0.4)	2	(0.4)
Back Pain	13	(4.6)	10	(3.5)	23	(4.1)
Bursitis	1	(0.4)	0	(0.0)	1	(0.2)
Costochondritis	1	(0.4)	0	(0.0)	1	(0.2)
Exostosis	1	(0.4)	0	(0.0)	1	(0.2)
Gouty Arthritis	1	(0.4)	0	(0.0)	1	(0.2)
Groin Pain	1	(0.4)	0	(0.0)	1	(0.2)
Intervertebral Disc Protrusion	0	(0.0)	1	(0.4)	1	(0.2)
Jaw Cyst	1	(0.4)	0	(0.0)	1	(0.2)
Joint Swelling	1	(0.4)	0	(0.0)	1	(0.2)
Muscle Spasms	2	(0.7)	3	(1.1)	5	(0.9)
Muscular Weakness	2	(0.7)	0	(0.0)	2	(0.4)
Musculoskeletal Chest Pain	3	(1.1)	0	(0.0)	3	(0.5)
Musculoskeletal Pain	1	(0.4)	7	(2.5)	8	(1.4)
Musculoskeletal Stiffness	1	(0.4)	0	(0.0)	1	(0.2)
Myalgia	3	(1.1)	5	(1.8)	8	(1.4)
Myopathy	1	(0.4)	0	(0.0)	1	(0.2)
Neck Pain	5	(1.8)	0	(0.0)	5	(0.9)
Osteonecrosis	0	(0.0)	1	(0.4)	1	(0.2)
Osteopenia	0	(0.0)	2	(0.7)	2	(0.4)
Osteoporosis	1	(0.4)	1	(0.4)	2	(0.4)

Number (%) of Patients With Specific Clinical Adverse Experiences
(Incidence >0% in One or More Treatment Groups) by System Organ Class - All Events - Moderate or Severe - Double-Blind Phase, All Available Data

	Raltegravir 400 mg b.i.d. (N = 281)		Efavirenz 600 mg q.h.s. (N = 282)		Total (N = 563)	
	n	(%)	n	(%)	n	(%)
Musculoskeletal And Connective Tissue Disorders	43	(15.3)	45	(16.0)	88	(15.6)
Pain In Extremity	7	(2.5)	5	(1.8)	12	(2.1)
Rotator Cuff Syndrome	0	(0.0)	1	(0.4)	1	(0.2)
Sacroiliitis	0	(0.0)	1	(0.4)	1	(0.2)
Synovial Cyst	1	(0.4)	0	(0.0)	1	(0.2)
Tendonitis	2	(0.7)	1	(0.4)	3	(0.5)
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	12	(4.3)	18	(6.4)	30	(5.3)
Anal Cancer	0	(0.0)	2	(0.7)	2	(0.4)
Anogenital Warts	3	(1.1)	4	(1.4)	7	(1.2)
Basal Cell Carcinoma	1	(0.4)	1	(0.4)	2	(0.4)
Bone Neoplasm Malignant	0	(0.0)	1	(0.4)	1	(0.2)
Breast Cancer	2	(0.7)	0	(0.0)	2	(0.4)
Castleman's Disease	1	(0.4)	0	(0.0)	1	(0.2)
Fibroadenoma Of Breast	0	(0.0)	1	(0.4)	1	(0.2)
Kaposi's Sarcoma AIDS Related	2	(0.7)	4	(1.4)	6	(1.1)
Lung Cancer Metastatic	1	(0.4)	0	(0.0)	1	(0.2)
Lung Neoplasm Malignant	1	(0.4)	0	(0.0)	1	(0.2)
Plasmablastic Lymphoma	0	(0.0)	1	(0.4)	1	(0.2)
Skin Papilloma	2	(0.7)	3	(1.1)	5	(0.9)
Uterine Leiomyoma	0	(0.0)	1	(0.4)	1	(0.2)
Nervous System Disorders	57	(20.3)	58	(20.6)	115	(20.4)
Balance Disorder	0	(0.0)	1	(0.4)	1	(0.2)

Number (%) of Patients With Specific Clinical Adverse Experiences
(Incidence >0% in One or More Treatment Groups) by System Organ Class - All Events - Moderate or Severe - Double-Blind Phase, All Available Data

	Raltegravir 400 mg b.i.d. (N = 281)		Efavirenz 600 mg q.h.s. (N = 282)		Total (N = 563)	
	n	(%)	n	(%)	n	(%)
Nervous System Disorders	57	(20.3)	58	(20.6)	115	(20.4)
Burning Sensation	0	(0.0)	1	(0.4)	1	(0.2)
Carotid Artery Occlusion	0	(0.0)	1	(0.4)	1	(0.2)
Carpal Tunnel Syndrome	3	(1.1)	0	(0.0)	3	(0.5)
Cerebral Haemorrhage	1	(0.4)	0	(0.0)	1	(0.2)
Cervical Root Pain	1	(0.4)	0	(0.0)	1	(0.2)
Cognitive Disorder	0	(0.0)	1	(0.4)	1	(0.2)
Convulsion	1	(0.4)	2	(0.7)	3	(0.5)
Coordination Abnormal	0	(0.0)	1	(0.4)	1	(0.2)
Dizziness	9	(3.2)	22	(7.8)	31	(5.5)
Dystonia	0	(0.0)	1	(0.4)	1	(0.2)
Encephalitis	1	(0.4)	0	(0.0)	1	(0.2)
Headache	29	(10.3)	28	(9.9)	57	(10.1)
Hyperreflexia	1	(0.4)	0	(0.0)	1	(0.2)
Hypersomnia	1	(0.4)	1	(0.4)	2	(0.4)
Hypoaesthesia	2	(0.7)	2	(0.7)	4	(0.7)
Memory Impairment	1	(0.4)	0	(0.0)	1	(0.2)
Mental Impairment	0	(0.0)	1	(0.4)	1	(0.2)
Migraine	5	(1.8)	2	(0.7)	7	(1.2)
Nervous System Disorder	0	(0.0)	1	(0.4)	1	(0.2)
Neuralgia	1	(0.4)	0	(0.0)	1	(0.2)
Neuropathy Peripheral	0	(0.0)	1	(0.4)	1	(0.2)

Number (%) of Patients With Specific Clinical Adverse Experiences
(Incidence >0% in One or More Treatment Groups) by System Organ Class - All Events - Moderate or Severe - Double-Blind Phase, All Available Data

	Raltegravir 400 mg b.i.d. (N = 281)		Efavirenz 600 mg q.h.s. (N = 282)		Total (N = 563)	
	n	(%)	n	(%)	n	(%)
Nervous System Disorders	57	(20.3)	58	(20.6)	115	(20.4)
Paraesthesia	1	(0.4)	3	(1.1)	4	(0.7)
Polyneuropathy	0	(0.0)	1	(0.4)	1	(0.2)
Poor Quality Sleep	1	(0.4)	0	(0.0)	1	(0.2)
Post Herpetic Neuralgia	1	(0.4)	1	(0.4)	2	(0.4)
Restless Legs Syndrome	1	(0.4)	0	(0.0)	1	(0.2)
Sciatica	1	(0.4)	1	(0.4)	2	(0.4)
Sedation	0	(0.0)	1	(0.4)	1	(0.2)
Sinus Headache	1	(0.4)	1	(0.4)	2	(0.4)
Somnolence	1	(0.4)	5	(1.8)	6	(1.1)
Syncope	1	(0.4)	3	(1.1)	4	(0.7)
Tension Headache	1	(0.4)	0	(0.0)	1	(0.2)
Transient Ischaemic Attack	0	(0.0)	1	(0.4)	1	(0.2)
VIIth Nerve Paralysis	4	(1.4)	0	(0.0)	4	(0.7)
Psychiatric Disorders	48	(17.1)	51	(18.1)	99	(17.6)
Abnormal Dreams	5	(1.8)	5	(1.8)	10	(1.8)
Affect Lability	0	(0.0)	1	(0.4)	1	(0.2)
Anhedonia	0	(0.0)	1	(0.4)	1	(0.2)
Anxiety	5	(1.8)	15	(5.3)	20	(3.6)
Confusional State	1	(0.4)	0	(0.0)	1	(0.2)
Conversion Disorder	0	(0.0)	2	(0.7)	2	(0.4)
Depressed Mood	0	(0.0)	2	(0.7)	2	(0.4)

Number (%) of Patients With Specific Clinical Adverse Experiences
(Incidence >0% in One or More Treatment Groups) by System Organ Class - All Events - Moderate or Severe - Double-Blind Phase, All Available Data

	Raltegravir 400 mg b.i.d. (N = 281)		Efavirenz 600 mg q.h.s. (N = 282)		Total (N = 563)	
	n	(%)	n	(%)	n	(%)
Psychiatric Disorders	48	(17.1)	51	(18.1)	99	(17.6)
Depression	18	(6.4)	12	(4.3)	30	(5.3)
Disorientation	0	(0.0)	2	(0.7)	2	(0.4)
Drug Abuse	1	(0.4)	1	(0.4)	2	(0.4)
Hallucination, Visual	0	(0.0)	1	(0.4)	1	(0.2)
Insomnia	16	(5.7)	18	(6.4)	34	(6.0)
Libido Decreased	3	(1.1)	0	(0.0)	3	(0.5)
Loss Of Libido	0	(0.0)	2	(0.7)	2	(0.4)
Major Depression	2	(0.7)	0	(0.0)	2	(0.4)
Mental Disorder	2	(0.7)	1	(0.4)	3	(0.5)
Nervousness	1	(0.4)	0	(0.0)	1	(0.2)
Nightmare	5	(1.8)	3	(1.1)	8	(1.4)
Panic Attack	1	(0.4)	1	(0.4)	2	(0.4)
Post-Traumatic Stress Disorder	1	(0.4)	0	(0.0)	1	(0.2)
Psychosomatic Disease	1	(0.4)	0	(0.0)	1	(0.2)
Psychotic Disorder	1	(0.4)	0	(0.0)	1	(0.2)
Schizoaffective Disorder	0	(0.0)	1	(0.4)	1	(0.2)
Sleep Disorder	0	(0.0)	2	(0.7)	2	(0.4)
Stress	0	(0.0)	1	(0.4)	1	(0.2)
Suicidal Behaviour	0	(0.0)	1	(0.4)	1	(0.2)
Suicidal Ideation	1	(0.4)	1	(0.4)	2	(0.4)
Suicide Attempt	4	(1.4)	0	(0.0)	4	(0.7)

Number (%) of Patients With Specific Clinical Adverse Experiences
(Incidence >0% in One or More Treatment Groups) by System Organ Class - All Events - Moderate or Severe - Double-Blind Phase, All Available Data

	Raltegravir 400 mg b.i.d. (N = 281)		Efavirenz 600 mg q.h.s. (N = 282)		Total (N = 563)	
	n	(%)	n	(%)	n	(%)
Renal And Urinary Disorders	7	(2.5)	12	(4.3)	19	(3.4)
Calculus Urinary	0	(0.0)	1	(0.4)	1	(0.2)
Dysuria	3	(1.1)	1	(0.4)	4	(0.7)
Haematuria	2	(0.7)	0	(0.0)	2	(0.4)
Hydronephrosis	0	(0.0)	1	(0.4)	1	(0.2)
Nephrolithiasis	3	(1.1)	3	(1.1)	6	(1.1)
Pollakiuria	2	(0.7)	1	(0.4)	3	(0.5)
Proteinuria	0	(0.0)	1	(0.4)	1	(0.2)
Renal Colic	0	(0.0)	4	(1.4)	4	(0.7)
Renal Failure	0	(0.0)	1	(0.4)	1	(0.2)
Urinary Bladder Haemorrhage	0	(0.0)	1	(0.4)	1	(0.2)
Urinary Tract Pain	1	(0.4)	0	(0.0)	1	(0.2)
Reproductive System And Breast Disorders	10	(3.6)	15	(5.3)	25	(4.4)
Balanitis	0	(0.0)	2	(0.7)	2	(0.4)
Breast Pain	0	(0.0)	1	(0.4)	1	(0.2)
Epididymitis	0	(0.0)	1	(0.4)	1	(0.2)
Erectile Dysfunction	8	(2.8)	3	(1.1)	11	(2.0)
Genital Lesion	0	(0.0)	1	(0.4)	1	(0.2)
Menorrhagia	0	(0.0)	1	(0.4)	1	(0.2)
Ovarian Cyst	1	(0.4)	1	(0.4)	2	(0.4)
Prostatitis	0	(0.0)	1	(0.4)	1	(0.2)
Testicular Pain	1	(0.4)	0	(0.0)	1	(0.2)

Number (%) of Patients With Specific Clinical Adverse Experiences
(Incidence >0% in One or More Treatment Groups) by System Organ Class - All Events - Moderate or Severe - Double-Blind Phase, All Available Data

	Raltegravir 400 mg b.i.d. (N = 281)		Efavirenz 600 mg q.h.s. (N = 282)		Total (N = 563)	
	n	(%)	n	(%)	n	(%)
Reproductive System And Breast Disorders	10	(3.6)	15	(5.3)	25	(4.4)
Uterine Haemorrhage	0	(0.0)	1	(0.4)	1	(0.2)
Vaginal Discharge	0	(0.0)	1	(0.4)	1	(0.2)
Vaginal Haemorrhage	0	(0.0)	1	(0.4)	1	(0.2)
Vulval Disorder	0	(0.0)	1	(0.4)	1	(0.2)
Respiratory, Thoracic And Mediastinal Disorders	37	(13.2)	27	(9.6)	64	(11.4)
Asthma	2	(0.7)	3	(1.1)	5	(0.9)
Bronchial Hyperreactivity	1	(0.4)	0	(0.0)	1	(0.2)
Chronic Obstructive Pulmonary Disease	1	(0.4)	1	(0.4)	2	(0.4)
Cough	15	(5.3)	8	(2.8)	23	(4.1)
Dyspnoea	3	(1.1)	4	(1.4)	7	(1.2)
Dyspnoea Exertional	1	(0.4)	0	(0.0)	1	(0.2)
Epistaxis	1	(0.4)	0	(0.0)	1	(0.2)
Haemoptysis	0	(0.0)	1	(0.4)	1	(0.2)
Hypoxia	1	(0.4)	0	(0.0)	1	(0.2)
Lung Disorder	1	(0.4)	0	(0.0)	1	(0.2)
Nasal Congestion	2	(0.7)	2	(0.7)	4	(0.7)
Nasal Dryness	0	(0.0)	1	(0.4)	1	(0.2)
Oropharyngeal Pain	7	(2.5)	3	(1.1)	10	(1.8)
Paranasal Sinus Hypersecretion	0	(0.0)	1	(0.4)	1	(0.2)
Pharyngeal Erythema	0	(0.0)	1	(0.4)	1	(0.2)
Pleural Effusion	1	(0.4)	2	(0.7)	3	(0.5)

Number (%) of Patients With Specific Clinical Adverse Experiences
(Incidence >0% in One or More Treatment Groups) by System Organ Class - All Events - Moderate or Severe - Double-Blind Phase, All Available Data

	Raltegravir 400 mg b.i.d. (N = 281)		Efavirenz 600 mg q.h.s. (N = 282)		Total (N = 563)	
	n	(%)	n	(%)	n	(%)
Respiratory, Thoracic And Mediastinal Disorders	37	(13.2)	27	(9.6)	64	(11.4)
Pleuritic Pain	0	(0.0)	1	(0.4)	1	(0.2)
Productive Cough	2	(0.7)	0	(0.0)	2	(0.4)
Pulmonary Congestion	0	(0.0)	1	(0.4)	1	(0.2)
Respiratory Failure	1	(0.4)	0	(0.0)	1	(0.2)
Rhinitis Allergic	6	(2.1)	2	(0.7)	8	(1.4)
Rhinorrhoea	1	(0.4)	0	(0.0)	1	(0.2)
Sinus Congestion	3	(1.1)	4	(1.4)	7	(1.2)
Sleep Apnoea Syndrome	1	(0.4)	0	(0.0)	1	(0.2)
Sneezing	1	(0.4)	0	(0.0)	1	(0.2)
Tachypnoea	1	(0.4)	0	(0.0)	1	(0.2)
Upper Respiratory Tract Congestion	2	(0.7)	1	(0.4)	3	(0.5)
Upper-Airway Cough Syndrome	1	(0.4)	1	(0.4)	2	(0.4)
Skin And Subcutaneous Tissue Disorders	35	(12.5)	51	(18.1)	86	(15.3)
Acne	5	(1.8)	1	(0.4)	6	(1.1)
Alopecia	2	(0.7)	1	(0.4)	3	(0.5)
Alopecia Areata	0	(0.0)	2	(0.7)	2	(0.4)
Blister	0	(0.0)	1	(0.4)	1	(0.2)
Dermatitis	0	(0.0)	1	(0.4)	1	(0.2)
Dermatitis Allergic	2	(0.7)	2	(0.7)	4	(0.7)
Dermatitis Contact	2	(0.7)	1	(0.4)	3	(0.5)
Drug Eruption	0	(0.0)	2	(0.7)	2	(0.4)

Number (%) of Patients With Specific Clinical Adverse Experiences
(Incidence >0% in One or More Treatment Groups) by System Organ Class - All Events - Moderate or Severe - Double-Blind Phase, All Available Data

	Raltegravir 400 mg b.i.d. (N = 281)		Efavirenz 600 mg q.h.s. (N = 282)		Total (N = 563)	
	n	(%)	n	(%)	n	(%)
Skin And Subcutaneous Tissue Disorders	35	(12.5)	51	(18.1)	86	(15.3)
Eczema	0	(0.0)	1	(0.4)	1	(0.2)
Eosinophilic Pustular Folliculitis	1	(0.4)	0	(0.0)	1	(0.2)
Erythema	0	(0.0)	1	(0.4)	1	(0.2)
Heat Rash	1	(0.4)	0	(0.0)	1	(0.2)
Hyperhidrosis	1	(0.4)	1	(0.4)	2	(0.4)
Intertrigo	1	(0.4)	1	(0.4)	2	(0.4)
Lipoatrophy	1	(0.4)	0	(0.0)	1	(0.2)
Lipohypertrophy	1	(0.4)	0	(0.0)	1	(0.2)
Macule	1	(0.4)	0	(0.0)	1	(0.2)
Nail Bed Inflammation	0	(0.0)	1	(0.4)	1	(0.2)
Night Sweats	3	(1.1)	0	(0.0)	3	(0.5)
Papule	2	(0.7)	1	(0.4)	3	(0.5)
Petechiae	0	(0.0)	1	(0.4)	1	(0.2)
Photosensitivity Reaction	1	(0.4)	0	(0.0)	1	(0.2)
Pruritus	3	(1.1)	2	(0.7)	5	(0.9)
Pruritus Generalised	2	(0.7)	0	(0.0)	2	(0.4)
Rash	6	(2.1)	14	(5.0)	20	(3.6)
Rash Generalised	0	(0.0)	1	(0.4)	1	(0.2)
Rash Macular	0	(0.0)	2	(0.7)	2	(0.4)
Rash Maculo-Papular	0	(0.0)	8	(2.8)	8	(1.4)
Rash Papular	0	(0.0)	2	(0.7)	2	(0.4)

Number (%) of Patients With Specific Clinical Adverse Experiences
(Incidence >0% in One or More Treatment Groups) by System Organ Class - All Events - Moderate or Severe - Double-Blind Phase, All Available Data

	Raltegravir 400 mg b.i.d. (N = 281)		Efavirenz 600 mg q.h.s. (N = 282)		Total (N = 563)	
	n	(%)	n	(%)	n	(%)
Skin And Subcutaneous Tissue Disorders	35	(12.5)	51	(18.1)	86	(15.3)
Rosacea	0	(0.0)	1	(0.4)	1	(0.2)
Seborrhoeic Dermatitis	2	(0.7)	1	(0.4)	3	(0.5)
Skin Exfoliation	0	(0.0)	1	(0.4)	1	(0.2)
Skin Hyperpigmentation	0	(0.0)	2	(0.7)	2	(0.4)
Skin Lesion	2	(0.7)	2	(0.7)	4	(0.7)
Swelling Face	0	(0.0)	2	(0.7)	2	(0.4)
Urticaria	2	(0.7)	0	(0.0)	2	(0.4)
Vascular Disorders	11	(3.9)	9	(3.2)	20	(3.6)
Arteriosclerosis Obliterans	0	(0.0)	1	(0.4)	1	(0.2)
Deep Vein Thrombosis	1	(0.4)	0	(0.0)	1	(0.2)
Hot Flush	0	(0.0)	1	(0.4)	1	(0.2)
Hypertension	8	(2.8)	7	(2.5)	15	(2.7)
Hypertensive Crisis	1	(0.4)	0	(0.0)	1	(0.2)
Pallor	1	(0.4)	0	(0.0)	1	(0.2)

Although a patient may have had two or more clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

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Table S6. Change in baseline metabolic parameters by treatment group*

			Change From Baseline at Week 240		RAL – EFV	
Treatment Group	N	Baseline Mean	Mean Change (SD)	(95% CI)	Difference (95% CI)	p-Value
Fasting serum cholesterol (mg/dL)						
RAL	207	158.8	16.01 (33.34)	(11.45, 20.58)	-27.3 (-34.5, -20.1)	<0.001
EFV	187	157.1	44.01 (44.04)	(37.65, 50.36)		
Fasting serum HDL-C (mg/dL)						
RAL	207	37.85	5.68 (9.01)	(4.44, 6.91)	-7.07 (-9.11, -5.04)	<0.001
EFV	187	38.37	12.62 (12.15)	(10.87, 14.37)		
Fasting serum LDL-C (mg/dL)						
RAL	204	96.19	9.92 (27.74)	(6.09, 13.75)	-14.2 (-20.2, -8.14)	<0.001
EFV	182	92.54	25.38 (36.00)	(20.12, 30.65)		
Fasting serum triglyceride (mg/dL)						
RAL	207	128.3	1.53 (83.32)	(-9.89, 12.95)	-36.5 (-61.4, -11.7)	0.004
EFV	187	140.6	37.26 (159.11)	(14.30, 60.21)		
Fasting serum glucose (mg/dL)						
RAL	205	91.87	4.04 (17.62)	(1.62, 6.47)	-1.99 (-4.97, 1.00)	0.191
EFV	187	90.88	6.26 (12.84)	(4.40, 8.11)		
Total:HDL-C ratio						
RAL	207	4.43	-0.22 (1.08)	(-0.36, -0.07)	-0.11 (-0.36, 0.14)	0.375
EFV	187	4.37	-0.08 (1.62)	(-0.31, 0.15)		
Non-HDL-C (mg/dL)						
RAL	207	121.0	10.34 (30.74)	(6.13, 14.55)	-20.3 (-27.4, -13.2)	<0.001
EFV	187	118.7	31.39 (43.85)	(25.06, 37.71)		

♦ See **Figure S2** for comparison of lipid values to NCEP goals.

† Within-group 95% confidence intervals (CI) were based on t-distribution.

‡ The 95% confidence intervals (CI) and p-values for treatment difference were calculated from an ANOCOVA model with terms for baseline lipid level and treatment.

N = Number of patients in the treatment group.

The Last-Observation-Carried-Forward approach was applied for missing data because of increased lipids (such as the addition lipid-lowering medications).

Figure S1. **Time to first-reported adverse neuropsychiatric experience.**

Time to neuropsychiatric symptoms was defined as the time between randomization and the onset of first nervous system adverse experience in the expanded list (2). A patient with a single neuropsychiatric symptom and a patient with several neuropsychiatric side-effects of diverse types were each tallied once in the composite frequency analysis of patients with neuropsychiatric adverse experiences on the basis of the first reported event. The time to the first reported neuropsychiatric event was significantly longer for raltegravir than efavirenz recipients (log-rank p <0.001).

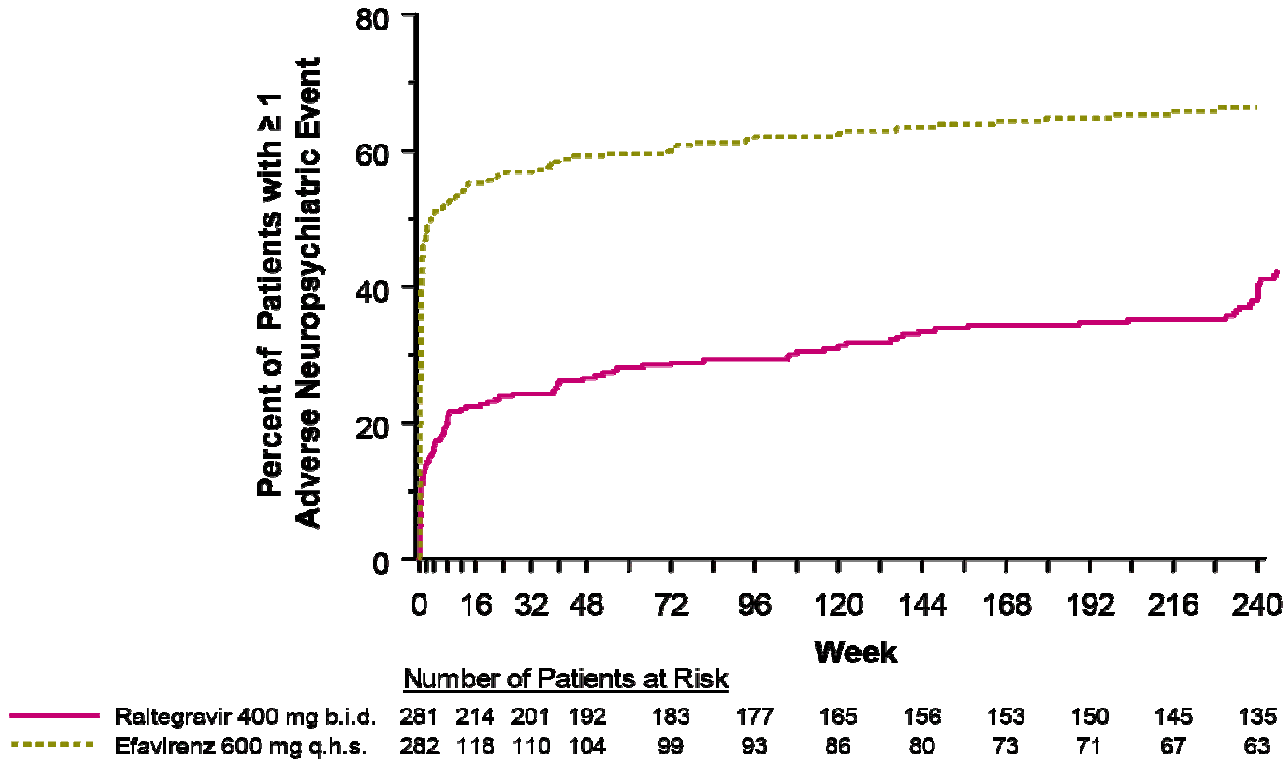

Figure S2. Lipid values at baseline and at Week 240 by treatment group contrasted with NCEP targets.